```
Connecting via Winsock to Dialog at dialog.com on port 23


Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ********
ENTER PASSWORD:
 ********
Welcome to DIALOG

Dialog level 05.31.00D

Last logoff:  30jan12 10:54:26
Logon file405 30jan12 10:54:27
DETAIL set on
HILIGHT set on as '****'
COST        = SHORT.
MEDIOBAB is set ON as an alias for 155, 347, 144, 35, 5, 74, 71, 357, 6,
351, 24, 136, 399, 315, 358, 73, 34, 434
FISH is set ON as an alias for 10, 143, 203, 50, 28, 35, 351, 24, 136, 44,
399, 78
NUTRACEUT is set ON as an alias for 79, 164, 91, 53, 51, 351, 399, 467,149
MEDBIOFT is set ON as an alias for 349, 444, 457
* * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.8.0 term=ASCII
                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

    (c) 2003 Dialog, a Thomson business.      All rights reserved.

      /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b mediobab

>>>         357 does not exist
>>>         358 does not exist
>>>2 of the specified files are not available
      30jan12 10:54:35 User226352 Session D1340.1
     $0.00  Estimated cost FileHomeBase
     $0.05  TELNET
     $0.05  Estimated cost this search
```

```
     $0.05  Estimated total session cost   0.291 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1950-2012/Jan 27
         (c) format only 2012 Dialog
*File 155: Medline has resumed updating with UD20111205. Updates going
forward will have the 2012 MeSH Thesaurus applied. See ?NEWS154.
  File 347:JAPIO Dec 1976-2011/OCT(Updated 120125)
         (c) 2012 JPO & JAPIO
  File 144:Pascal 1973-2012/Jan W4
         (c) 2012 INIST/CNRS
*File 144: Please see HELP NEWS144 for important information on
recent update processing.
  File  35:Dissertation Abs Online 1861-2011/Dec
         (c) 2012 ProQuest Info&Learning
  File   5:Biosis Previews(R) 1926-2012/Jan W4
         (c) 2012 The Thomson Corporation
  File  74:Int.Pharm.Abs 1970-2012/Jan B2
         (c) 2012 The Thomson Corporation
  File  71:ELSEVIER BIOBASE 1994-2012/Jan W5
         (c) 2012 Elsevier B.V.
  File   6:NTIS 1964-2012/Jan W4
         (c) 2012 NTIS, Intl Cpyrght All Rights Res
  File 351:Derwent WPI 1963-2012/UD=201206
         (c) 2012 Thomson Reuters
  File  24:CSA Life Sciences Abstracts 1966-2012/Jan
         (c) 2012 CSA.
  File 136:BioEngineering Abstracts 1966-2007/Jan
         (c) 2007 CSA.
*File 136: This file is closed.
  File 399:CA SEARCH(R) 1967-2012/UD=15605
         (c) 2012 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.
  File 315:ChemEng & Biotec Abs 1970-2011/May
         (c) 2011 DECHEMA
*File 315: Chemical Engineering and Biotechnology Abstracts has ceased
updating effective May 2011.  No further updates are expected.
  File  73:EMBASE 1974-2012/Jan 30
         (c) 2012 Elsevier B.V.
  File  34:SciSearch(R) Cited Ref Sci 1990-2012/Jan W4
         (c) 2012 The Thomson Corp
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 2006 The Thomson Corp

      Set  Items  Description
      ---  -----  -----------
? s ((protective (w) antigen) or PA) and ((monophosphoryl (w)lipid(w)A or mpl)
>>>Unmatched parentheses
? s ((protective (w) antigen) or PA) and ((monophosphoryl (w)lipid(w)A) or mpl)

155: MEDLINE(R)_1950-2012/Jan 27
Processing
          650  MONOPHOSPHORYL
       284502  LIPID
     12495965  A
          615  MONOPHOSPHORYL(W)LIPID(W)A
         1935  MPL
       172926  PROTECTIVE
       456718  ANTIGEN
         1693  PROTECTIVE(W)ANTIGEN
      1971140  PA
```

```
           333  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
             6  MONOPHOSPHORYL
          4488  LIPID
       9046843  A
             5  MONOPHOSPHORYL(W)LIPID(W)A
            65  MPL
         92453  PROTECTIVE
          7008  ANTIGEN
            11  PROTECTIVE(W)ANTIGEN
         14147  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

144: Pascal_1973-2012/Jan W4
           307  MONOPHOSPHORYL
        109392  LIPID
      11813487  A
           293  MONOPHOSPHORYL(W)LIPID(W)A
          1133  MPL
         83072  PROTECTIVE
        180539  ANTIGEN
           746  PROTECTIVE(W)ANTIGEN
         40375  PA
            11  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 35: Dissertation Abs Online_1861-2011/Dec
            29  MONOPHOSPHORYL
         13866  LIPID
       1853979  A
            25  MONOPHOSPHORYL(W)LIPID(W)A
           101  MPL
         11860  PROTECTIVE
         12015  ANTIGEN
           108  PROTECTIVE(W)ANTIGEN
          4484  PA
             1  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

  5: Biosis Previews(R)_1926-2012/Jan W4
Processing
           763  MONOPHOSPHORYL
        339789  LIPID
      12644998  A
           717  MONOPHOSPHORYL(W)LIPID(W)A
          2301  MPL
        156336  PROTECTIVE
        433448  ANTIGEN
          2167  PROTECTIVE(W)ANTIGEN
         53775  PA
            15  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 74: Int.Pharm.Abs_1970-2012/Jan B2
            24  MONOPHOSPHORYL
          9255  LIPID
        382498  A
            24  MONOPHOSPHORYL(W)LIPID(W)A
            29  MPL
```

```
          4034  PROTECTIVE
          2485  ANTIGEN
            18  PROTECTIVE(W)ANTIGEN
           682  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
           332  MONOPHOSPHORYL
        123696  LIPID
       4200794  A
           316  MONOPHOSPHORYL(W)LIPID(W)A
          1029  MPL
         72023  PROTECTIVE
        132191  ANTIGEN
          1006  PROTECTIVE(W)ANTIGEN
         16083  PA
            14  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

  6: NTIS_1964-2012/Jan W4
            16  MONOPHOSPHORYL
          2387  LIPID
       1851411  A
            16  MONOPHOSPHORYL(W)LIPID(W)A
           121  MPL
         22911  PROTECTIVE
          4540  ANTIGEN
           189  PROTECTIVE(W)ANTIGEN
         20832  PA
             3  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

351: Derwent WPI_1963-2012/UD=201206
Processing
Processing
           477  MONOPHOSPHORYL
         49031  LIPID
      19525243  A
           417  MONOPHOSPHORYL(W)LIPID(W)A
           852  MPL
        408316  PROTECTIVE
         59963  ANTIGEN
           466  PROTECTIVE(W)ANTIGEN
         55538  PA
            41  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 24: CSA Life Sciences Abstracts_1966-2012/Jan
           369  MONOPHOSPHORYL
         68234  LIPID
       3924805  A
           346  MONOPHOSPHORYL(W)LIPID(W)A
           609  MPL
         62433  PROTECTIVE
        232850  ANTIGEN
          1370  PROTECTIVE(W)ANTIGEN
         10871  PA
            13  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

136: BioEngineering Abstracts_1966-2007/Jan
```

```
             4  MONOPHOSPHORYL
          2012  LIPID
        146587  A
             4  MONOPHOSPHORYL(W)LIPID(W)A
             9  MPL
          1010  PROTECTIVE
          1997  ANTIGEN
            19  PROTECTIVE(W)ANTIGEN
           481  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

399: CA SEARCH(R)_1967-2012/UD=15605
           305  MONOPHOSPHORYL
        274265  LIPID
       4006895  A  (AMPERE(UNIT))
           281  MONOPHOSPHORYL(W)LIPID(W)A
          1346  MPL
        133766  PROTECTIVE
        301597  ANTIGEN
          1320  PROTECTIVE(W)ANTIGEN
         11843  PA
             2  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

315: ChemEng & Biotec Abs_1970-2011/May
             4  MONOPHOSPHORYL
          1803  LIPID
        387792  A
             3  MONOPHOSPHORYL(W)LIPID(W)A
            41  MPL
          4531  PROTECTIVE
          1700  ANTIGEN
            19  PROTECTIVE(W)ANTIGEN
          3686  PA
             1  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 73: EMBASE_1974-2012/Jan 30
Processing
           664  MONOPHOSPHORYL
        385388  LIPID
      13563202  A
           618  MONOPHOSPHORYL(W)LIPID(W)A
          2001  MPL
        186047  PROTECTIVE
        776626  ANTIGEN
          1726  PROTECTIVE(W)ANTIGEN
         71852  PA
            26  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                (W)LIPID(W)A) OR MPL)

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
Processing
           886  MONOPHOSPHORYL
        290475  LIPID
      15431444  A
           860  MONOPHOSPHORYL(W)LIPID(W)A
          3341  MPL
        150565  PROTECTIVE
        354804  ANTIGEN
          2127  PROTECTIVE(W)ANTIGEN
```

```
          64032  PA
             28  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                 (W)LIPID(W)A) OR MPL)

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
             30  MONOPHOSPHORYL
          42028  LIPID
        1450745  A
             28  MONOPHOSPHORYL(W)LIPID(W)A
             14  MPL
           8853  PROTECTIVE
          65544  ANTIGEN
             97  PROTECTIVE(W)ANTIGEN
           1476  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                 (W)LIPID(W)A) OR MPL)

TOTAL: FILES 155,347,144 and ...
        1571136  PROTECTIVE
        3024025  ANTIGEN
          13082  PROTECTIVE(W)ANTIGEN
        2341297  PA
           4866  MONOPHOSPHORYL
        2000611  LIPID
      112726688  A
           4568  MONOPHOSPHORYL(W)LIPID(W)A
          14927  MPL
     S1     488  ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                 (W)LIPID(W)A) OR MPL)
? s s1 not PY>2005

155: MEDLINE(R)_1950-2012/Jan 27
            333  S1
        4598344  PY>2005
            198  S1 NOT PY>2005

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
              0  S1
        1779777  PY>2005
              0  S1 NOT PY>2005

144: Pascal_1973-2012/Jan W4
             11  S1
        2808894  PY>2005
              6  S1 NOT PY>2005

 35: Dissertation Abs Online_1861-2011/Dec
              1  S1
         373944  PY>2005
              0  S1 NOT PY>2005

  5: Biosis Previews(R)_1926-2012/Jan W4
             15  S1
        3848067  PY>2005
             11  S1 NOT PY>2005

 74: Int.Pharm.Abs_1970-2012/Jan B2
              0  S1
         116155  PY>2005
              0  S1 NOT PY>2005

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
```

```
             14  S1
        2014424  PY>2005
              7  S1 NOT PY>2005

  6: NTIS_1964-2012/Jan W4
              3  S1
         132351  PY>2005
              3  S1 NOT PY>2005

351: Derwent WPI_1963-2012/UD=201206
Processing
             41  S1
        8689536  PY>2005
              5  S1 NOT PY>2005

 24: CSA Life Sciences Abstracts_1966-2012/Jan
             13  S1
        1459373  PY>2005
             10  S1 NOT PY>2005

136: BioEngineering Abstracts_1966-2007/Jan
              0  S1
           2459  PY>2005
              0  S1 NOT PY>2005

399: CA SEARCH(R)_1967-2012/UD=15605
              2  S1
        6592170  PY>2005
              0  S1 NOT PY>2005

315: ChemEng & Biotec Abs_1970-2011/May
              1  S1
          44433  PY>2005
              1  S1 NOT PY>2005

 73: EMBASE_1974-2012/Jan 30
             26  S1
        5117126  PY>2005
             17  S1 NOT PY>2005

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
             28  S1
        8261188  PY>2005
             17  S1 NOT PY>2005

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
              0  S1
              0  PY>2005
              0  S1 NOT PY>2005

TOTAL: FILES 155,347,144 and ...
            488  S1
       45838241  PY>2005
     S2     275  S1 NOT PY>2005
? s ((protective (w) antigen) or PA) and (chiotosan)

155: MEDLINE(R)_1950-2012/Jan 27
              1  CHIOTOSAN
         172926  PROTECTIVE
         456718  ANTIGEN
           1693  PROTECTIVE(W)ANTIGEN
        1971140  PA
```

```
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
             0  CHIOTOSAN
         92453  PROTECTIVE
          7008  ANTIGEN
            11  PROTECTIVE(W)ANTIGEN
         14147  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

144: Pascal_1973-2012/Jan W4
             1  CHIOTOSAN
         83072  PROTECTIVE
        180539  ANTIGEN
           746  PROTECTIVE(W)ANTIGEN
         40375  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 35: Dissertation Abs Online_1861-2011/Dec
             0  CHIOTOSAN
         11860  PROTECTIVE
         12015  ANTIGEN
           108  PROTECTIVE(W)ANTIGEN
          4484  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

  5: Biosis Previews(R)_1926-2012/Jan W4
             0  CHIOTOSAN
        156336  PROTECTIVE
        433448  ANTIGEN
          2167  PROTECTIVE(W)ANTIGEN
         53775  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 74: Int.Pharm.Abs_1970-2012/Jan B2
             0  CHIOTOSAN
          4034  PROTECTIVE
          2485  ANTIGEN
            18  PROTECTIVE(W)ANTIGEN
           682  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
             0  CHIOTOSAN
         72023  PROTECTIVE
        132191  ANTIGEN
          1006  PROTECTIVE(W)ANTIGEN
         16083  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

  6: NTIS_1964-2012/Jan W4
             0  CHIOTOSAN
         22911  PROTECTIVE
          4540  ANTIGEN
           189  PROTECTIVE(W)ANTIGEN
         20832  PA
             0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

351: Derwent WPI_1963-2012/UD=201206
             2  CHIOTOSAN
        408316  PROTECTIVE
         59963  ANTIGEN
```

```
            466  PROTECTIVE(W)ANTIGEN
          55538  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 24: CSA Life Sciences Abstracts_1966-2012/Jan
              1  CHIOTOSAN
          62433  PROTECTIVE
         232850  ANTIGEN
           1370  PROTECTIVE(W)ANTIGEN
          10871  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

136: BioEngineering Abstracts_1966-2007/Jan
              0  CHIOTOSAN
           1010  PROTECTIVE
           1997  ANTIGEN
             19  PROTECTIVE(W)ANTIGEN
            481  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

399: CA SEARCH(R)_1967-2012/UD=15605
              0  CHIOTOSAN
         133766  PROTECTIVE
         301597  ANTIGEN
           1320  PROTECTIVE(W)ANTIGEN
          11843  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

315: ChemEng & Biotec Abs_1970-2011/May
              0  CHIOTOSAN
           4531  PROTECTIVE
           1700  ANTIGEN
             19  PROTECTIVE(W)ANTIGEN
           3686  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 73: EMBASE_1974-2012/Jan 30
              2  CHIOTOSAN
         186047  PROTECTIVE
         776626  ANTIGEN
           1726  PROTECTIVE(W)ANTIGEN
          71852  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
              1  CHIOTOSAN
         150565  PROTECTIVE
         354804  ANTIGEN
           2127  PROTECTIVE(W)ANTIGEN
          64032  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
              0  CHIOTOSAN
           8853  PROTECTIVE
          65544  ANTIGEN
             97  PROTECTIVE(W)ANTIGEN
           1476  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)

TOTAL: FILES 155,347,144 and ...
        1571136  PROTECTIVE
```

```
        3024025  ANTIGEN
          13082  PROTECTIVE(W)ANTIGEN
        2341297  PA
              8  CHIOTOSAN
      S3      0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)
? s
>>>Null command ignored
? s ((protective (w) antigen) or PA) and (chitosan)

155: MEDLINE(R)_1950-2012/Jan 27
          8773  CHITOSAN
        172926  PROTECTIVE
        456718  ANTIGEN
          1693  PROTECTIVE(W)ANTIGEN
       1971140  PA
           515  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
          2781  CHITOSAN
         92453  PROTECTIVE
          7008  ANTIGEN
            11  PROTECTIVE(W)ANTIGEN
         14147  PA
             1  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

144: Pascal_1973-2012/Jan W4
         10109  CHITOSAN
         83072  PROTECTIVE
        180539  ANTIGEN
           746  PROTECTIVE(W)ANTIGEN
         40375  PA
            44  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 35: Dissertation Abs Online_1861-2011/Dec
           489  CHITOSAN
         11860  PROTECTIVE
         12015  ANTIGEN
           108  PROTECTIVE(W)ANTIGEN
          4484  PA
             3  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

  5: Biosis Previews(R)_1926-2012/Jan W4
         11388  CHITOSAN
        156336  PROTECTIVE
        433448  ANTIGEN
          2167  PROTECTIVE(W)ANTIGEN
         53775  PA
            56  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 74: Int.Pharm.Abs_1970-2012/Jan B2
          4034  PROTECTIVE
          2485  ANTIGEN
            18  PROTECTIVE(W)ANTIGEN
           682  PA
          1972  CHITOSAN
             4  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
          3850  CHITOSAN
         72023  PROTECTIVE
        132191  ANTIGEN
          1006  PROTECTIVE(W)ANTIGEN
```

```
          16083  PA
             20  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

  6: NTIS_1964-2012/Jan W4
            134  CHITOSAN
          22911  PROTECTIVE
           4540  ANTIGEN
            189  PROTECTIVE(W)ANTIGEN
          20832  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

351: Derwent WPI_1963-2012/UD=201206
          19554  CHITOSAN
         408316  PROTECTIVE
          59963  ANTIGEN
            466  PROTECTIVE(W)ANTIGEN
          55538  PA
            258  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 24: CSA Life Sciences Abstracts_1966-2012/Jan
           5192  CHITOSAN
          62433  PROTECTIVE
         232850  ANTIGEN
           1370  PROTECTIVE(W)ANTIGEN
          10871  PA
             19  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

136: BioEngineering Abstracts_1966-2007/Jan
           1010  PROTECTIVE
           1997  ANTIGEN
             19  PROTECTIVE(W)ANTIGEN
            481  PA
            804  CHITOSAN
              3  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

399: CA SEARCH(R)_1967-2012/UD=15605
         133766  PROTECTIVE
         301597  ANTIGEN
           1320  PROTECTIVE(W)ANTIGEN
          11843  PA
          32948  CHITOSAN
             10  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

315: ChemEng & Biotec Abs_1970-2011/May
            828  CHITOSAN
           4531  PROTECTIVE
           1700  ANTIGEN
             19  PROTECTIVE(W)ANTIGEN
           3686  PA
              4  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 73: EMBASE_1974-2012/Jan 30
          12519  CHITOSAN
         186047  PROTECTIVE
         776626  ANTIGEN
           1726  PROTECTIVE(W)ANTIGEN
          71852  PA
            127  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
          22077  CHITOSAN
         150565  PROTECTIVE
```

```
         354804  ANTIGEN
           2127  PROTECTIVE(W)ANTIGEN
          64032  PA
            116  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
            527  CHITOSAN
           8853  PROTECTIVE
          65544  ANTIGEN
             97  PROTECTIVE(W)ANTIGEN
           1476  PA
              0  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)

TOTAL: FILES 155,347,144 and ...
        1571136  PROTECTIVE
        3024025  ANTIGEN
          13082  PROTECTIVE(W)ANTIGEN
        2341297  PA
         133945  CHITOSAN
     S4    1180  ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)
? s s4 not PY>2005

155: MEDLINE(R)_1950-2012/Jan 27
             515  S4
         4598344  PY>2005
             144  S4 NOT PY>2005

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
               1  S4
         1779777  PY>2005
               1  S4 NOT PY>2005

144: Pascal_1973-2012/Jan W4
              44  S4
         2808894  PY>2005
              17  S4 NOT PY>2005

 35: Dissertation Abs Online_1861-2011/Dec
               3  S4
          373944  PY>2005
               0  S4 NOT PY>2005

  5: Biosis Previews(R)_1926-2012/Jan W4
              56  S4
         3848067  PY>2005
              18  S4 NOT PY>2005

 74: Int.Pharm.Abs_1970-2012/Jan B2
               4  S4
          116155  PY>2005
               0  S4 NOT PY>2005

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
              20  S4
         2014424  PY>2005
               7  S4 NOT PY>2005

  6: NTIS_1964-2012/Jan W4
               0  S4
          132351  PY>2005
               0  S4 NOT PY>2005
```

```
351: Derwent WPI_1963-2012/UD=201206
Processing
           258  S4
       8689536  PY>2005
            32  S4 NOT PY>2005

 24: CSA Life Sciences Abstracts_1966-2012/Jan
            19  S4
       1459373  PY>2005
             4  S4 NOT PY>2005

136: BioEngineering Abstracts_1966-2007/Jan
             3  S4
          2459  PY>2005
             2  S4 NOT PY>2005

399: CA SEARCH(R)_1967-2012/UD=15605
            10  S4
       6592170  PY>2005
             1  S4 NOT PY>2005

315: ChemEng & Biotec Abs_1970-2011/May
             4  S4
         44433  PY>2005
             3  S4 NOT PY>2005

 73: EMBASE_1974-2012/Jan 30
           127  S4
       5117126  PY>2005
            41  S4 NOT PY>2005

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
           116  S4
       8261188  PY>2005
            35  S4 NOT PY>2005

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
             0  S4
             0  PY>2005
             0  S4 NOT PY>2005

TOTAL: FILES 155,347,144 and ...
          1180  S4
      45838241  PY>2005
     S5    305  S4 NOT PY>2005
? ds

Set   File    Items   Description
      155       333
      347         0
      144        11
       35         1
        5        15
       74         0
       71        14
        6         3
      351        41
       24        13
      136         0
      399         2
      315         1
       73        26
```

```
        34         28
       434          0
S1                488   ((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL
                    (W)LIPID(W)A) OR MPL)
       155        198
       347          0
       144          6
        35          0
         5         11
        74          0
        71          7
         6          3
       351          5
        24         10
       136          0
       399          0
       315          1
        73         17
        34         17
       434          0
S2                275   S1 NOT PY>2005
       155          0
       347          0
       144          0
        35          0
         5          0
        74          0
        71          0
         6          0
       351          0
        24          0
       136          0
       399          0
       315          0
        73          0
        34          0
       434          0
S3                  0   ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)
       155        515
       347          1
       144         44
        35          3
         5         56
        74          4
        71         20
         6          0
       351        258
        24         19
       136          3
       399         10
       315          4
        73        127
        34        116
       434          0
S4                1180   ((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)
       155        144
       347          1
       144         17
        35          0
         5         18
        74          0
        71          7
```

```
        6          0
      351         32
       24          4
      136          2
      399          1
      315          3
       73         41
       34         35
      434          0
S5               305   S4 NOT PY>2005
? rd s5

>>>Duplicate detection is not supported for File 347.

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
      S6     241  RD S5  (unique items)
? rd s2

>>>Duplicate detection is not supported for File 347.

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
      S7     219  RD S2  (unique items)
? rd s2

>>>Duplicate detection is not supported for File 347.

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
      S8     219  RD S2  (unique items)
? s s6 and s7

155: MEDLINE(R)_1950-2012/Jan 27
             144  S6
             198  S7
               0  S6 AND S7

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
               0  S7
               1  S6
               0  S6 AND S7

144: Pascal_1973-2012/Jan W4
               0  S7
              13  S6
               0  S6 AND S7

 35: Dissertation Abs Online_1861-2011/Dec
               0  S7
               0  S6
               0  S6 AND S7

  5: Biosis Previews(R)_1926-2012/Jan W4
               0  S7
               5  S6
               0  S6 AND S7

 74: Int.Pharm.Abs_1970-2012/Jan B2
```

```
                0  S7
                0  S6
                0  S6 AND S7

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
                0  S7
                1  S6
                0  S6 AND S7

  6: NTIS_1964-2012/Jan W4
                0  S6
                2  S7
                0  S6 AND S7

351: Derwent WPI_1963-2012/UD=201206
                5  S7
               32  S6
                0  S6 AND S7

 24: CSA Life Sciences Abstracts_1966-2012/Jan
                1  S6
                1  S7
                0  S6 AND S7

136: BioEngineering Abstracts_1966-2007/Jan
                0  S7
                0  S6
                0  S6 AND S7

399: CA SEARCH(R)_1967-2012/UD=15605
                0  S7
                1  S6
                0  S6 AND S7

315: ChemEng & Biotec Abs_1970-2011/May
                1  S7
                3  S6
                0  S6 AND S7

 73: EMBASE_1974-2012/Jan 30
                5  S7
               25  S6
                0  S6 AND S7

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
                7  S7
               15  S6
                0  S6 AND S7

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
                0  S7
                0  S6
                0  S6 AND S7

TOTAL: FILES 155,347,144 and ...
              241  S6
              219  S7
      S9        0  S6 AND S7
? ds

Set   File    Items   Description
      155       333
```

	347	0	
	144	11	
	35	1	
	5	15	
	74	0	
	71	14	
	6	3	
	351	41	
	24	13	
	136	0	
	399	2	
	315	1	
	73	26	
	34	28	
	434	0	
S1		488	((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL (W)LIPID(W)A) OR MPL)
	155	198	
	347	0	
	144	6	
	35	0	
	5	11	
	74	0	
	71	7	
	6	3	
	351	5	
	24	10	
	136	0	
	399	0	
	315	1	
	73	17	
	34	17	
	434	0	
S2		275	S1 NOT PY>2005
	155	0	
	347	0	
	144	0	
	35	0	
	5	0	
	74	0	
	71	0	
	6	0	
	351	0	
	24	0	
	136	0	
	399	0	
	315	0	
	73	0	
	34	0	
	434	0	
S3		0	((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)
	155	515	
	347	1	
	144	44	
	35	3	
	5	56	
	74	4	
	71	20	
	6	0	
	351	258	
	24	19	
	136	3	

	399	10	
	315	4	
	73	127	
	34	116	
	434	0	
S4		1180	((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)
	155	144	
	347	1	
	144	17	
	35	0	
	5	18	
	74	0	
	71	7	
	6	0	
	351	32	
	24	4	
	136	2	
	399	1	
	315	3	
	73	41	
	34	35	
	434	0	
S5		305	S4 NOT PY>2005
	155	144	
	347	1	
	144	13	
	35	0	
	5	5	
	74	0	
	71	1	
	6	0	
	351	32	
	24	1	
	136	0	
	399	1	
	315	3	
	73	25	
	34	15	
	434	0	
S6		241	RD S5 (unique items)
	155	198	
	347	0	
	144	0	
	35	0	
	5	0	
	74	0	
	71	0	
	6	2	
	351	5	
	24	1	
	136	0	
	399	0	
	315	1	
	73	5	
	34	7	
	434	0	
S7		219	RD S2 (unique items)
	155	198	
	347	0	
	144	0	
	35	0	
	5	0	

```
        74          0
        71          0
         6          2
       351          5
        24          1
       136          0
       399          0
       315          1
        73          5
        34          7
       434          0
S8                219   RD S2  (unique items)
       155          0
       347          0
       144          0
        35          0
         5          0
        74          0
        71          0
         6          0
       351          0
        24          0
       136          0
       399          0
       315          0
        73          0
        34          0
       434          0
S9                  0   S6 AND S7
? s s6 or s7

155: MEDLINE(R)_1950-2012/Jan 27
             144  S6
             198  S7
             342  S6 OR S7

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
               0  S7
               1  S6
               1  S6 OR S7

144: Pascal_1973-2012/Jan W4
               0  S7
              13  S6
              13  S6 OR S7

 35: Dissertation Abs Online_1861-2011/Dec
               0  S7
               0  S6
               0  S6 OR S7

  5: Biosis Previews(R)_1926-2012/Jan W4
               0  S7
               5  S6
               5  S6 OR S7

 74: Int.Pharm.Abs_1970-2012/Jan B2
               0  S7
               0  S6
               0  S6 OR S7

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
```

```
              0  S7
              1  S6
              1  S6 OR S7

  6: NTIS_1964-2012/Jan W4
              0  S6
              2  S7
              2  S6 OR S7

351: Derwent WPI_1963-2012/UD=201206
              5  S7
             32  S6
             37  S6 OR S7

 24: CSA Life Sciences Abstracts_1966-2012/Jan
              1  S6
              1  S7
              2  S6 OR S7

136: BioEngineering Abstracts_1966-2007/Jan
              0  S7
              0  S6
              0  S6 OR S7

399: CA SEARCH(R)_1967-2012/UD=15605
              0  S7
              1  S6
              1  S6 OR S7

315: ChemEng & Biotec Abs_1970-2011/May
              1  S7
              3  S6
              4  S6 OR S7

 73: EMBASE_1974-2012/Jan 30
              5  S7
             25  S6
             30  S6 OR S7

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
              7  S7
             15  S6
             22  S6 OR S7

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
              0  S7
              0  S6
              0  S6 OR S7

TOTAL: FILES 155,347,144 and ...
            241  S6
            219  S7
     S10    460  S6 OR S7
? s s10 and (antrax or anthracis)

155: MEDLINE(R)_1950-2012/Jan 27
            342  S10
             28  ANTRAX
           4347  ANTHRACIS
              6  S10 AND (ANTRAX OR ANTHRACIS)

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
```

```
              1  S10
             19  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

144: Pascal_1973-2012/Jan W4
             13  S10
             30  ANTRAX
           1888  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

 35: Dissertation Abs Online_1861-2011/Dec
              0  S10
            286  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

  5: Biosis Previews(R)_1926-2012/Jan W4
              5  S10
              5  ANTRAX
           5815  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

 74: Int.Pharm.Abs_1970-2012/Jan B2
              0  S10
             53  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

 71: ELSEVIER BIOBASE_1994-2012/Jan W5
              1  S10
           2004  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

  6: NTIS_1964-2012/Jan W4
              2  S10
            748  ANTHRACIS
              1  S10 AND (ANTRAX OR ANTHRACIS)

351: Derwent WPI_1963-2012/UD=201206
             37  S10
              6  ANTRAX
           1270  ANTHRACIS
              3  S10 AND (ANTRAX OR ANTHRACIS)

 24: CSA Life Sciences Abstracts_1966-2012/Jan
              2  S10
              2  ANTRAX
           2299  ANTHRACIS
              1  S10 AND (ANTRAX OR ANTHRACIS)

136: BioEngineering Abstracts_1966-2007/Jan
              0  S10
            130  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

399: CA SEARCH(R)_1967-2012/UD=15605
              1  S10
              8  ANTRAX
           4299  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

315: ChemEng & Biotec Abs_1970-2011/May
              4  S10
             46  ANTHRACIS
```

```
              0  S10 AND (ANTRAX OR ANTHRACIS)

 73: EMBASE_1974-2012/Jan 30
             30  S10
             22  ANTRAX
           4846  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
             22  S10
              2  ANTRAX
           3863  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
              0  S10
            136  ANTHRACIS
              0  S10 AND (ANTRAX OR ANTHRACIS)

TOTAL: FILES 155,347,144 and ...
            460  S10
            103  ANTRAX
          32049  ANTHRACIS
     S11      11  S10 AND (ANTRAX OR ANTHRACIS)
? s s10 and (anthrax or anthracis)

155: MEDLINE(R)_1950-2012/Jan 27
            342  S10
           5505  ANTHRAX
           4347  ANTHRACIS
              7  S10 AND (ANTHRAX OR ANTHRACIS)

347: JAPIO_Dec 1976-2011/OCT(Updated 120125)
              1  S10
             17  ANTHRAX
             19  ANTHRACIS
              0  S10 AND (ANTHRAX OR ANTHRACIS)

144: Pascal_1973-2012/Jan W4
             13  S10
           1654  ANTHRAX
           1888  ANTHRACIS
              1  S10 AND (ANTHRAX OR ANTHRACIS)

 35: Dissertation Abs Online_1861-2011/Dec
              0  S10
            271  ANTHRAX
            286  ANTHRACIS
              0  S10 AND (ANTHRAX OR ANTHRACIS)

  5: Biosis Previews(R)_1926-2012/Jan W4
              5  S10
           5437  ANTHRAX
           5815  ANTHRACIS
              0  S10 AND (ANTHRAX OR ANTHRACIS)

 74: Int.Pharm.Abs_1970-2012/Jan B2
              0  S10
            153  ANTHRAX
             53  ANTHRACIS
              0  S10 AND (ANTHRAX OR ANTHRACIS)
```

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 71: ELSEVIER BIOBASE_1994-2012/Jan W5
               1  S10
            2087  ANTHRAX
            2004  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

  6: NTIS_1964-2012/Jan W4
               2  S10
             875  ANTHRAX
             748  ANTHRACIS
               1  S10 AND (ANTHRAX OR ANTHRACIS)

351: Derwent WPI_1963-2012/UD=201206
              37  S10
            1745  ANTHRAX
            1270  ANTHRACIS
               4  S10 AND (ANTHRAX OR ANTHRACIS)

 24: CSA Life Sciences Abstracts_1966-2012/Jan
               2  S10
            1999  ANTHRAX
            2299  ANTHRACIS
               1  S10 AND (ANTHRAX OR ANTHRACIS)

136: BioEngineering Abstracts_1966-2007/Jan
               0  S10
             133  ANTHRAX
             130  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

399: CA SEARCH(R)_1967-2012/UD=15605
               1  S10
            3136  ANTHRAX
            4299  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

315: ChemEng & Biotec Abs_1970-2011/May
               4  S10
              44  ANTHRAX
              46  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

 73: EMBASE_1974-2012/Jan 30
              30  S10
            6424  ANTHRAX
            4846  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

 34: SciSearch(R) Cited Ref Sci_1990-2012/Jan W4
              22  S10
            4235  ANTHRAX
            3863  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
               0  S10
             222  ANTHRAX
             136  ANTHRACIS
               0  S10 AND (ANTHRAX OR ANTHRACIS)

TOTAL: FILES 155,347,144 and ...
             460  S10
```

```
          33937  ANTHRAX
          32049  ANTHRACIS
     S12      14  S10 AND (ANTHRAX OR ANTHRACIS)
? t s12/7/all

 12/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2012 Dialog. All rts. reserv.

17022644   PMID: 16019195
   Efficacy of non-toxic deletion mutants of ****protective****
****antigen**** from Bacillus ****anthracis****.
  Rhie Gi-eun; Park Young-Mia; Han Ji-Sun; Yu Jae-Yon; Seong Won-Keun; Oh
Hee-Bok
  Department of Microbiology, National Institute of Health, 194 Tongil-Lo,
Seoul 122-701, Republic of Korea. gerhie@nih.go.kr
  FEMS immunology and medical microbiology (Netherlands)  Aug 1 2005,  45
 (2)  p341-7,  ISSN  0928-8244--Print  0928-8244--Linking  Journal Code:
9315554
  Publishing Model Print
  Document type: Journal Article; Research Support, Non-U.S. Gov't
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Current human ****anthrax**** vaccines available in the United States and
Europe consist of alum-precipitated supernatant material from cultures of a
toxigenic, nonencapsulated strain of Bacillus ****anthracis****. The major
component of human ****anthrax**** vaccine that confers protection is
****protective****  ****antigen**** (****PA****). A second-generation human
vaccine using the recombinant ****PA**** (rPA) is being developed. In this
study, to prevent the toxicity and the degradation of the native rPA by
proteases, we constructed two ****PA**** variants, delPA (163-168) and
delPA (313-314), that lack trypsin (S(163)-R(164)-K(165)-K(166)-R(167)-S(16
8)) or chymotrypsin cleavage sequence (F(313)-F(314)), respectively. These
proteins were expressed in Bacillus brevis 47-5Q. The delPAs were
fractionated from the culture supernatant of B. brevis by ammonium sulfate
at 70% saturation, followed by anion exchange chromatography on a Hitrap Q,
Hiload 16/60 superdex 200 gel filtration column and phenyl sepharose
hydrophobic interaction column. In accordance with previous reports, both
delPA proteins combined with lethal factor protein did not show any
cytotoxicity on J774A.1 cells. The delPA (163-168) and delPA (313-314)
formulated either in Rehydragel HPA or ****MPL****-TDM-CWS (Ribi-Trimix),
elicited a comparable amount of anti-****PA**** and neutralizing antibodies
to those of native rPA in guinea pigs, and confers full protection of
guinea pigs from 50xLD50 of fully virulent B. ****anthracis**** spore
challenges. Ribi-Trimix was significantly more effective in inducing anti-
****PA****  and neutralizing antibodies than Rehydragel HPA. These results
indicate the possibility of delPA (163-168) and delPA (313-314) proteins
being developed into nontoxic, effective and stable recombinant vaccine
candidates.
  Record Date Created: 20050729
  Record Date Completed: 20051027


 12/7/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2012 Dialog. All rts. reserv.

17022642   PMID: 16009541
   Expression and secretion of the ****protective**** ****antigen**** of
Bacillus ****anthracis**** in Bacillus brevis.
  Rhie Gi-Eun; Park Young-Mia; Chun Jeong-Hoon; Yoo Cheon-Kwon; Seong
```

Won-Keun; Oh Hee-Bok
Department of Microbiology, National Institute of Health, 194 Tongil-Lo, Seoul 122-701, Korea.
FEMS immunology and medical microbiology (Netherlands) Aug 1 2005, 45 (2) p331-9, ISSN 0928-8244--Print 0928-8244--Linking Journal Code: 9315554
Publishing Model Print
Document type: In Vitro; Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We used the Bacillus brevis-pNU212 system to develop a mass production system for the ****protective**** ****antigen**** (****PA****) of Bacillus ****anthracis****. A moderately efficient expression-secretion system for ****PA**** was constructed by fusing the ****PA**** gene from B. ****anthracis**** with the B. brevis cell-wall protein signal-peptide encoding region of pNU212, and by introducing the recombinant plasmid, pNU212-mPA, into B. brevis 47-5Q. The clone producing ****PA**** secreted about 300 microg of recombinant ****PA**** (rPA) per ml of 5PY-erythromycin medium after 4 days incubation at 30 degrees C. The rPA was fractionated from the culture supernatant of B. brevis 47-5Q carrying pNU212-mPA using ammonium sulfate at 70% saturation followed by anion exchange chromatography on a Hitrap Q, a Hiload 16/60 Superdex 200 gel filtration column and a phenyl sepharose hydrophobic interaction column, yielding 70 mg rPA per liter of culture. The N-terminal sequence of the purified rPA was identical to that of native ****PA**** from B. ****anthracis****. The purified rPA exhibited cytotoxicity towards J774A.1 cells when combined with lethal factor. The rPA formulated in either Rehydragel HPA or ****MPL**** -TDM-CWS adjuvant (Ribi-Trimix) elicited the expression of a large amount of anti-****PA**** and neutralizing antibodies in guinea pigs and completely protected them against a 100 LD50 challenge with fully virulent B. ****anthracis**** spores.
Record Date Created: 20050729
Record Date Completed: 20051027

12/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

16320257 PMID: 15193401
Pluronic F127-based systemic vaccine delivery systems.
Coeshott Claire M; Smithson S Louise; Verderber Evie; Samaniego Adrian; Blonder Joan M; Rosenthal Gary J; Westerink M A Julie
RxKinetix Inc., 1172 Century Drive Suite 260, Louisville, CO 80027, USA. ccoeshott@rxkinetix.com
Vaccine (Netherlands) Jun 23 2004, 22 (19) p2396-405, ISSN 0264-410X--Print 0264-410X--Linking Journal Code: 8406899
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We have developed a vaccine delivery system based on the non-ionic block copolymer, Pluronic F127 (F127), combined with selected immunomodulators. F127-based matrices are characterized by a phenomenon known as reverse thermogelation, whereby the formulation undergoes a phase transition from liquid to gel upon reaching physiological temperatures. Protein antigens (tetanus toxoid (TT), diphtheria toxoid (DT) and ****anthrax**** recombinant ****protective**** ****antigen**** (rPA)) were formulated with F127 in combination with CpG motifs or ****chitosan****, as examples of

immunomodulators, and were compared to more traditional adjuvants in mice. IgG antibody responses were significantly enhanced by the F127/CpG and F127/****chitosan**** combinations compared to antigens mixed with CpGs or ****chitosan**** alone. In addition, the responses were significantly greater than those elicited by aluminum salts. Furthermore, the functional activity of these antibodies was demonstrated using either in vivo tetanus toxin challenge or an ****anthrax**** lethal toxin neutralization assay. These studies suggest that a block-copolymer approach could enhance the delivery of a variety of clinically useful antigens in vaccination schemes.
Record Date Created: 20040614
Record Date Completed: 20040907

12/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13236428 PMID: 9682372
Comparative efficacy of experimental ****anthrax**** vaccine candidates against inhalation ****anthrax**** in rhesus macaques.
Ivins B E; Pitt M L; Fellows P F; Farchaus J W; Benner G E; Waag D M; Little S F; Anderson G W; Gibbs P H; Friedlander A M
Bacteriology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21702-5011, USA. bruce ivins@detrick.army.mil
Vaccine (ENGLAND) Jul 1998, 16 (11-12) p1141-8, ISSN 0264-410X--Print 0264-410X--Linking Journal Code: 8406899
Publishing Model Print
Document type: Comparative Study; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The authors examined the efficacy of Bacillus ****anthracis**** ****protective**** ****antigen**** (****PA****) combined with adjuvants as vaccines against an aerosol challenge of virulent ****anthrax**** spores in rhesus macaques. Adjuvants tested included i) aluminum hydroxide (Alhydrogel), ii) saponin QS-21 and iii) ****monophosphoryl**** ****lipid**** ****A**** (****MPL****) in squalene/lecithin/Tween 80 emulsion (SLT). Animals were immunized once with either 50 micrograms of recombinant ****PA**** plus adjuvant, or with ****Anthrax**** Vaccine Adsorbed (AVA), the licensed human ****anthrax**** vaccine. The serological response to ****PA**** was measured by enzyme linked immunosorbent assay. Lymphocyte proliferation and serum neutralization of in vitro lethal toxin cytotoxicity were also assayed. In all vaccine groups, anti-****PA**** IgM and IgG titers peaked at 2 weeks and 4-5 weeks postimmunization, respectively. Five weeks postimmunization, animals in all vaccine groups demonstrated ****PA**** -specific lymphocyte proliferation and sera that neutralized in vitro cytotoxicity. Six weeks after immunization, the animals were challenged by aerosol with approximately 93 LD50 of virulent ****anthrax**** spores. Animals were bled daily for 1 week to monitor bacteremia, and deaths were recorded. Anti-****PA**** ELISA titers in all groups of immunized animals were substantially increased 2 weeks after challenge. One dose of each vaccine provided significant protection (> 90%) against inhalation ****anthrax**** in the rhesus macaques.
Record Date Created: 19981022
Record Date Completed: 19981022

12/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13185294 PMID: 9627938

Protective efficacy of a recombinant ****protective**** ****antigen**** against Bacillus ****anthracis**** challenge and assessment of immunological markers.

McBride B W; Mogg A; Telfer J L; Lever M S; Miller J; Turnbull P C; Baillie L

Centre for Applied Microbiology and Research, Porton Down, Salisbury, UK.

Vaccine (ENGLAND) May 1998, 16 (8) p810-7, ISSN 0264-410X--Print 0264-410X--Linking Journal Code: 8406899

Publishing Model Print

Document type: Comparative Study; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The efficacy of recombinant Bacillus ****anthracis**** ****Protective**** ****Antigen**** (rPA) produced in Bacillus subtilis and formulated in Alhydrogel or ****MPL**** -TDM-CWS (Ribi adjuvant) has been tested and compared to the licensed UK human vaccine in guinea pigs challenged by the aerosol route with the Ames strain of B. ****anthracis****. rPA combined with the Ribi adjuvant was found to be the only formulation to provide 100% protection from challenge. Analysis of immunological parameters in the individual animals revealed significant differences between the rPA/Ribi vaccine group and rPA/Alhydrogel and human vaccine groups for antigen specific lymphocyte proliferation, ****PA**** neutralisation and antigen specific IgG2 levels, but indicated no significant differences in ****PA**** -specific IgG1 levels. rPA formulated in Alhydrogel induced a mainly IgG1 response whilst the rPA/Ribi vaccine produced a predominantly IgG2 response.

Record Date Created: 19980921

Record Date Completed: 19980921

12/7/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12119792 PMID: 8701593

Experimental ****anthrax**** vaccines: efficacy of adjuvants combined with ****protective**** ****antigen**** against an aerosol Bacillus ****anthracis**** spore challenge in guinea pigs.

Ivins B; Fellows P; Pitt L; Estep J; Farchaus J; Friedlander A; Gibbs P

Bacteriology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21702-5011, USA.

Vaccine (ENGLAND) Dec 1995, 13 (18) p1779-84, ISSN 0264-410X--Print 0264-410X--Linking Journal Code: 8406899

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The efficacy of several human ****anthrax**** vaccine candidates comprised of different adjuvants together with Bacillus ****anthracis**** ****protective**** ****antigen**** (****PA****) was evaluated in guinea pigs challenged by an aerosol of virulent B. ****anthracis**** spores. The most efficacious vaccines tested were formulated with ****PA**** plus ****monophosphoryl**** ****lipid**** ****A**** (****MPL****) in a squalene/lecithin/Tween 80 emulsion (SLT) and ****PA**** plus the saponin QS-21. The ****PA****+****MPL**** in SLT vaccine, which was lyophilized and then reconstituted before use, demonstrated strong protective immunogenicity, even after storage for 2 years at 4 degrees C. The ****MPL**** component was required for maximum efficacy of the vaccine. Eliminating lyophilization of the vaccine did not diminish its protective

efficacy. No significant alteration in efficacy was observed when ****PA**** was dialyzed against different buffers before preparation of vaccine ***.*PA****+****MPL**** in SLT proved superior in efficacy to the licensed United States human ****anthrax**** vaccine in the guinea pig model.

Record Date Created: 19960904

Record Date Completed: 19960904

12/7/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10519542 PMID: 1730501 Record Identifier: PMC257681

Immunization against ****anthrax**** with Bacillus ****anthracis**** ****protective**** ****antigen**** combined with adjuvants.

Ivins B E; Welkos S L; Little S F; Crumrine M H; Nelson G O

Bacteriology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland 21702-5011.

Infection and immunity (UNITED STATES) Feb 1992, 60 (2) p662-8, ISSN 0019-9567--Print 0019-9567--Linking Journal Code: 0246127

Publishing Model Print; Cites Am J Public Health Nations Health. 1962 Apr;52(4):632-45 PMID 18017912; Cites Microb Pathog. 1989 Jul;7(1):15-35 PMID 2509851; Cites J Bacteriol. 1963 Jan;85:230-6 PMID 13972632; Cites Ann N Y Acad Sci. 1970 Oct 30;174(2):577-82 PMID 4993532; Cites J Immunol. 1954 Dec;73(6):387-91 PMID 13212061; Cites J Exp Med. 1954 Feb;99(2):167-82 PMID 13130792; Cites Lancet. 1991 Apr 27;337(8748):998-100 1 PMID 1673211; Cites Cancer Res. 1991 Nov 15;51(22):6045-51 PMID 1933867; Cites Infect Immun. 1991 Jun;59(6):1961-5 PMID 1903769; Cites Eur J Epidemiol. 1988 Mar;4(1):12-9 PMID 3128450; Cites Infect Immun. 1988 Jan;56(1):176-81 PMID 2826334; Cites Methods Enzymol. 1988;165:103-16 PMID 3148094; Cites Infect Immun. 1986 Nov;54(2):537-42 PMID 3021632; Cites Med Microbiol Immunol. 1988;177(5):293-303 PMID 3139974; Cites Cancer Res. 1988 Oct 15;48(20):5883-93 PMID 3262416; Cites Cancer Immunol Immunother. 1984;18(2):107-12 PMID 6391653; Cites J Immunol. 1984 Nov;133(5):2797-800 P MID 6332861; Cites Vaccine. 1987 Sep;5(3):223-8 PMID 3499713; Cites Infect Immun. 1985 Aug;49(2):291-7 PMID 3926644; Cites Adv Exp Med Biol. 1985;186:579-90 PMID 4050592; Cites Infect Immun. 1990 Feb;58(2):366-72 PMI D 2105271; Cites Infect Immun. 1990 Feb;58(2):303-8 PMID 2105269; Cites Infect Immun. 1984 Jan;43(1):337-40 PMID 6690408; Cites Appl Microbiol. 1963 Jul;11:330-4 PMID 13972634; Cites Microb Pathog. 1988 Aug;5(2):127-39 PMID 3148815; Cites Microb Pathog. 1988 Jan;4(1):53-69 PMID 3143893; Cites Infect Immun. 1986 May;52(2):509-12 PMID 3084385; Cites Infect Immun. 1986 May;52(2):454-8 PMID 3084383; Cites Infect Immun. 1986 May;52(2):356-63 PMID 3084381; Cites Infect Immun. 1986 Mar;51(3):795-800 PMID 3081444; Cites J Reticuloendothel Soc. 1979 Dec;26(Suppl):667-80 PMID 522085

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Other Citation Owner: NLM

Record type: MEDLINE; Completed

The protective efficacy of immunization against ****anthrax**** with Bacillus ****anthracis**** ****protective**** ****antigen**** (****PA****) combined with different adjuvants was tested in Hartley guinea pigs and CBA/J and A/J mice. Adjuvant components derived from microbial products that were tested included threonyl-muramyl dipeptide (threonyl-MDP); ****monophosphoryl**** ****lipid**** ****A**** (****MPL****); trehalose dimycolate (TDM); and the delipidated, deproteinized, cell wall skeleton (CWS) from either Mycobacterium phlei or the BCG strain of Mycobacterium bovis. Non-microbially derived adjuvants tested included aluminum hydroxide and the lipid amine CP-20,961. In guinea pigs, all adjuvants and adjuvant

mixtures enhanced antibody titers to ****PA**** as well as survival after a parenteral challenge of virulent B ***.*anthracis**** Ames spores. In contrast, ****PA**** alone or combined with either aluminum hydroxide or CP-20,961 failed to protect mice. Vaccines containing ****PA**** combined with threonyl-MDP or ****MPL**** -TDM-CWS protected a majority of female CBA/J mice. Statistical analysis of survival data in the guinea pigs indicated that ****PA****-****MPL****-CWS and ****PA****-****MPL**** -TDM-CWS were more efficacious than the currently licensed human ****anthrax**** vaccine.

Record Date Created: 19920218

Record Date Completed: 19920218

12/7/8 (Item 1 from file: 144)

DIALOG(R)File 144:Pascal

16864966 PASCAL No.: 04-0525824

Pluronic (R) F127-based systemic vaccine delivery systems

Modern Vaccine Adjuvants and Delivery Systems Meeting, Dublin, Ireland, 4-6 June 2003. Selected papers

COESHOTT Claire M; SMITHSON S Louise; VERDERBER Evie; SAMANIEGO Adrian; BLONDER Joan M; ROSENTHAL Gary J; WESTERINK M A Julie

MORROW W John W, ed; SHEIKH Nadeem A, ed

RxKinetix Inc., 1172 Century Drive Suite 260, Louisville, CO 80027, United States; Departments of Medicine and Pathology, Medical College of Ohio, Toledo, OH, United States

Washington National Primate Research Center, Departments of Pathobiology and Pharmaceutics, University of Washington, Seattle, WA 98121, United States

International MVADS Meeting, 1 (Dublin IRL) 2003-06-04

Journal: Vaccine, 2004, 22 (19) 2396-2405

ISSN: 0264-410X CODEN: VACCDE Availability: INIST-20289; 354000120008740070

No. of Refs.: 48 ref.

Document Type: P (Serial); C (Conference Proceedings) ; A (Analytic)

Country of Publication: United Kingdom

Language: English

We have developed a vaccine delivery system based on the non-ionic block copolymer, Pluronic (R) F127 (F127), combined with selected immunomodulators. F127-based matrices are characterized by a phenomenon known as reverse thermogelation, whereby the formulation undergoes a phase transition from liquid to gel upon reaching physiological temperature. Protein antigens (tetanus toxoid (TT), diphtheria toxoid (DT) and ****anthrax**** recombinant ****protective**** ****antigen**** (rPA)) were formulated with F127 in combination with CpG motifs or ****chitosan****. as examples of immunomodulators, and were compared to more traditional adjuvants in mice. IgG antibody responses were significantly enhanced by the F127/CpG and F127/****chitosan**** combinations compared to antigens mixed with CpGs or ****chitosan**** alone. In addition, the responses were significantly greater than those elicited by aluminum salts. Furthermore, the functional activity of these antibodies was demonstrated using either in vivo tetanus toxin challenge or an ****anthrax**** lethal toxin neutralization assay. These studies suggest that a block-copolymer approach could enhance the delivery of a variety of clinically useful antigens in vaccination schemes.

12/7/9 (Item 1 from file: 6)

DIALOG(R)File 6:NTIS

1918699 NTIS Accession Number: AD-A248 855/9
Immunization against ****Anthrax**** with Bacillus ****anthracis**** ****Protective**** ****Antigen**** Combined with Adjuvants. (Reannouncement with New Availability Information)
Ivins, B. E. ; Welkos, S. L. ; Little, S. F. ; Crumrine, M. H. ; Nelson, G. O.
Army Medical Research Inst. of Infectious Diseases, Fort Detrick, MD.
Corp. Source Codes: 029744000; 405039
Feb 92 7p
Languages: English Document Type: Journal article
Journal Announcement: GRAI9603
Pub. in Infection and Immunity, v60 n2 p662-668 Feb 92. Order this product from NTIS by: phone at 1-800-553-NTIS (U.S. customers); (703)605-6000 (other countries); fax at (703)321-8547; and email at orders@ntis.fedworld.gov. NTIS is located at 5285 Port Royal Road, Springfield, VA, 22161, USA.
NTIS Prices: PC A02/MF A01
Country of Publication: United States
The protective efficacy of immunization against ****anthrax**** with Bacillus ****anthracis**** ****protective**** ****antigen**** (****PA****) combined with different adjuvants was tested in Hartley guinea pigs and CBA/J and A/J mice. Adjuvant components derived from microbial products that were tested included threonyl-muramyl dipeptide (threonyl-MDP); ****monophosphoryl**** ****lipid**** ****A**** (****MPL****); trehalose dimycolate (TDM); and the delipidated, deproteinized, cell wall skeleton (CWS) from either Mycobacterium phlei or the BCG strain of Mycobacterium bovis. Non-microbially derived adjuvants tested included aluminum hydroxide and the lipid amine CP-20,961. In guinea pigs, all adjuvants and adjuvant mixtures enhanced antibody titers to ****PA**** as well as survival after a parenteral challenge of virulent B ***.*anthracis**** Ames spores. In contrast, ****PA**** alone or combined with either aluminum hydroxide or CP-20,961 failed to protect mice. Vaccines containing ****PA**** combined with threonyl-MDP or ****MPL**** -TDM-CWS protected a majority of female CBA/J mice. Statistical analysis of survival data in the guinea pigs indicated that ****PA****-****MPL****-CWS and ****PA****-****MPL**** -TDM-CWS were more efficacious than the currently licensed human ****anthrax**** vaccine.

12/7/10 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

0015128567
WPI ACC NO: 2005-478100/200548
XRAM Acc No: C2005-145630
New polynucleotide vaccine composition comprising a nucleic acid sequence that encodes a Bacillus ****anthracis**** antigen, useful for eliciting an immune response against B. ****anthracis**** in a subject
Patent Assignee: POWDERJECT VACCINES INC (POWD-N)
Inventor: FULLER J T; SCHMALJOHN C S
Patent Family (1 patents, 1 countries)

Patent Number	Kind	Date	Application Number	Kind	Date	Update
US 20050148529	A1	20050707	US 2004751103	A	20040105	200548 B

Priority Applications (no., kind, date): US 2004751103 A 20040105

Patent Details

Number	Kind	Lan	Pg	Dwg	Filing Notes

Alerting Abstract US A1

NOVELTY - A polynucleotide vaccine composition comprising a nucleic acid sequence that encodes a ~Bacillus ****anthracis**** ~ ****antigen****, where the nucleic acid sequence is operatively linked to a promoter for expression of the antigen in a mammalian cell, is new.

DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

1.a method for eliciting an immune response against

2.~B. ****anthracis****

3.~ in a ****subject****; and

4.a method for using a

5.~B. ****anthracis****

6.~ antigen to induce a protective immune ****response**** in a subject.

ACTIVITY - Immunostimulant. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful for eliciting an immune response against ~B. ****anthracis ~****.

Technology Focus

BIOTECHNOLOGY - Preferred Method: Eliciting an immune response against ~B. ****anthracis**** ~ ****in**** a subject, the method comprising administering the vaccine composition to the subject, where upon introduction to the subject, the nucleic acid sequence is expressed to provide the ~B. ****anthracis**** ~ antigen to ****elicit**** the immune response. The nucleic acid sequence is coated onto a core carrier particle and administered to the subject using a particle-mediated delivery technique. The method further comprises administering a second vaccine composition to the subject, which is an anti--B. ****anthracis**** ~ vaccine containing the peptide ****form**** of the ****Protective**** ****Antigen**** from ~B. ****anthracis**** ~. The ****second**** ****vaccine**** composition is administered ****to**** the subject in a boosting step. Both vaccine compositions are administered to the same site in the subject, concurrently. Both may be combined to provide a single composition. The nucleic acid sequence is present in a plasmid vector and encodes an antigen obtained or derived from the ****Protective**** ****Antigen**** of ~B. ****anthracis**** ~. The antigen encoded ****by**** ****the**** nucleic acid sequence ****is**** substantially homologous to the full-length ****Protective********Antigen**** protein. Specifically, the composition comprises a first nucleic ****acid********sequence**** that encodes a ~B. ****anthracis**** ~ antigen; and a second nucleic acid sequence that encodes a ****leader**** signal peptide operatively linked to the first nucleic acid sequence, where the first and the second nucleic acid sequences are operatively linked to a promoter for expression in a mammalian cell and the leader signal peptide provides for the secretion of the encoded antigen. The composition further comprises an adjuvant component present in the composition in the form of a nucleic acid sequence, i.e. CpG sequence. The adjuvant component is a further nucleic acid sequence that encodes a polypeptide adjuvant. The adjuvant component is present in the composition in a form other than a nucleic acid sequence, such as a polypeptide, a lipid, a non-protein hormone, or a vitamin, preferably****monophosphoryl********lipid********A****, saponin or its derivative, or Quil-A. The composition ****further********comprises**** ****a**** pharmaceutical excipient or vehicle. It is in particulate form.

The nucleic acid sequence is coated onto a core carrier particle. The core carrier particle has an average diameter of 0.1-10 mu. The core carrier particle comprises a metal, specifically gold. The composition may further comprise a transfection facilitating agent, and an adjuvant component described above. Using a ~B. ****anthracis**** ~ antigen to induce a protective immune response in a subject, the method ****comprises****: (a) providing an expression cassette containing a nucleic acid sequence encoding the ****Protective********Antigen**** from ~B. ****anthracis**** ~ operatively linked to control sequences that direct expression of ****the********Protective********Antigen**** when introduced ****into**** tissue of the subject; and (b) administering the expression cassette to ****tissue********of**** the subject such that the ****Protective**** ****Antigen**** is expressed to induce the protective immune response in the subject. The expression cassette ****is********present**** in a plasmid vector. The method may comprise: (a) providing an expression cassette containing a first nucleic acid sequence encoding the ****Protective**** ****Antigen**** from ~B. ****anthracis**** ~ and a second nucleic acid sequence that encodes a leader signal ****peptide****, ****where**** the first and ****second**** nucleic acid sequences are operatively linked to each other and to control sequences that direct expression of the sequences when introduced into tissue of the subject and the leader signal peptide provides for the secretion of the encoded ****Protective********Antigen**** ; and (b) administering the expression cassette to tissue of the subject such that the ****Protective********Antigen********is********expressed**** to induce the immune response in the subject. The leader signal peptide is the ****tissue********plasminogen**** activator (TPA) leader signal peptide. The plasmid vector is administered to the subject in particulate form. The plasmid vector is coated onto a core carrier particle and administered to the subject using a particle-mediated delivery technique.

Title Terms/Index Terms/Additional Words: NEW; POLYNUCLEOTIDE; VACCINE; COMPOSITION; COMPRISE; NUCLEIC; ACID; SEQUENCE; ENCODE; BACILLUS; ANTIGEN ; USEFUL; ELICIT; IMMUNE; RESPOND; SUBJECT

Class Codes
International Classification (+ Attributes)
IPC + Level Value Position Status Version

A61K-0039/07	A	I	R	20060101
A61K-0048/00	A	I	R	20060101
A61K-0039/07	C	I	R	20060101
A61K-0048/00	C	I	R	20060101

ICO: K61K-039:53, K61K-039:54, K61K-039:545, K61K-039:60
US Classification, Current Main: 514-044000; Secondary: 424-246100
US Classification, Issued: 51444, 424246.1

File Segment: CPI
DWPI Class: B04; C06; D16
Manual Codes (CPI/A-M): B04-B04C1; B04-E03F; B04-E08; B14-A01B; B14-S11B1; C04-B04C1; C04-E03F; C04-E08; C14-A01B; C14-S11B1; D05-H07

Original Publication Data by Authority

United States
Publication No. US 20050148529 A1 (Update 200548 B)
Publication Date: 20050707
Nucleic acid immunization
Assignee: Powderject Vaccines, Inc., Madison, WI, US (POWD-N)
Schmaljohn, Connie S., Fort Detrick, MD, US Residence: US Nationality: US
Fuller, James T., Middleton, WI, US Residence: US Nationality: US
Inventor: Schmaljohn, Connie S., Fort Detrick, MD, US Residence: US

Nationality: US
Fuller, James T., Middleton, WI, US Residence: US Nationality: US
Agent: BURNS DOANE SWECKER MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, US
Language: EN (40 pages, 3 drawings)
Application: US 2004751103 A 20040105 (Local application)
Original IPC: A61K-48/00(A) A61K-39/07(B)
Current IPC: A61K-39/07(R,A,I,M,EP,20060101,20060722,A)
A61K-39/07(R,I,M,EP,20060101,20060722,C)
A61K-48/00(R,I,M,EP,20060101,20051110,A)
A61K-48/00(R,I,M,EP,20060101,20051110,C)
Current ECLA ICO class: K61K-39:53 K61K-39:54 K61K-39:545 K61K-39:60
Current US Class (main): 514-044000
Current US Class (secondary): 424-246100
Original US Class (main): 51444
Original US Class (secondary): 424246.1
Original Abstract: Recombinant nucleic acid molecules are described. The molecules have a sequence or sequences encoding an antigen from ~Bacillus anthracis~. Vectors and compositions containing these molecules are also described. Methods for eliciting an immune response using these molecules and compositions are also described.
Claim:
1.
1. A polynucleotide vaccine composition comprising a nucleic acid sequence that encodes a ~Bacillus anthracis~ antigen, wherein said nucleic acid sequence is operatively linked to a promoter suitable for expression of the antigen in a mammalian cell.

12/7/11 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

0014904466
WPI ACC NO: 2005-252244/200526
Related WPI Acc No: 2003-697452; 2005-444089; 2008-A74027
XRAM Acc No: C2005-079795
Composition useful e.g. for the translocation of an effector (e.g. insulin) across a biological barrier, and for treatment of e.g. dementia and Parkinson's disease, comprises an effector and a counter ion to the effector
Patent Assignee: BEN-SASSON S A (BENS-I); COHEN E (COHE-I)
Inventor: BEN-SASSON S A; COHEN E
Patent Family (1 patents, 1 countries)

Patent Number	Kind	Date	Application Number	Kind	Date	Update
US 20050058702	A1	20050317	US 2003664989	A	20030917	200526 B

Priority Applications (no., kind, date): US 2003664989 A 20030917

Patent Details

Number	Kind	Lan	Pg	Dwg	Filing Notes
US 20050058702	A1	EN	12	0	

Alerting Abstract US A1
NOVELTY - Composition (A) for translocation of at least one effector across a biological barrier comprises at least one effector (I) and a counter ion (II) to (I).
DESCRIPTION - INDEPENDENT CLAIMS are also included for:

1.translocating at least one effector across a biological barrier comprising introducing (A) to a biological barrier and allowing (A) to translocate across the biological barrier, thereby translocating the at

least one effector across the biological barrier;

2.a method of mucosal vaccination comprising administering (A) (where the at least one effector comprises an antigen to which vaccination is desirable) to a subject;

3.a kit comprising (A) in one or more containers; and

4.preparation of (A).

ACTIVITY - Endocrine-Gen.; Antidiabetic; Antiinfertility; Osteopathic; Ophthalmological; Neuroprotective; Nootropic; Antiparkinsonian; Anticonvulsant; Cardiovascular-Gen.; Antiarteriosclerotic; Anticoagulant; Cardiant; Vasotropic; Cerebroprotective; Anorectic; Nephrotropic; Antianemic; Immunomodulator; Antirheumatic; Immunosuppressive; Antimicrobial; Virucide; Antibacterial; Fungicide; Antiparasitic; Cytostatic; Analgesic; Antidepressant; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - (A) is useful to translocate a variety of different substances (e.g. insulin) across a biological barrier regulated by tight junctions (e.g. mucosal epithelia). (A) is useful to treat or prevent a disease or pathological condition (endocrine disorders, diabetes, infertility, hormone deficiencies, osteoporosis, ophthalmological disorders, neurodegenerative disorders, Alzheimer's disease, dementia, Parkinson's disease, multiple sclerosis, Huntington's disease, cardiovascular disorders, atherosclerosis, hyper-coagulable states, hypo-coagulable states, coronary disease, cerebrovascular events, metabolic disorders, obesity, vitamin deficiencies, renal disorders, renal failure, hematological disorders, anemia of different entities, immunologic and rheumatologic disorders, autoimmune diseases, immune deficiencies, infectious diseases, viral infections, bacterial infections, fungal infections, parasitic infections, neoplastic diseases, multi-factorial disorders, impotence, chronic pain, depression, different fibrosis states and short stature) (all claimed). (A) is useful for mucosal vaccination. (A) is useful for administering monoclonal antibodies. No biological data given.

ADVANTAGE - (A) exhibits efficient, non-invasive delivery of an unaltered biologically active substance.

Technology Focus

PHARMACEUTICALS - Preparation: Preparation of (A) comprises lyophilizing (I) and (II) and reconstituting the lyophilized materials in an aqueous, partially aqueous or organic solvent, thereby producing the composition.

Preferred Components: (II) is an ionic liquid forming cation. (A) comprises an excipient and/or carrier. (A) is contained within a capsule. (A) may be in the form of a tablet, an aqueous dispersion, a cream, ointment or suppository and it is enteric-coated. (I) is an anionic impermeable molecule (a polysaccharide (a glycosaminoglycan (heparin, heparan sulfate, chondroitin sulfate, dermatan sulfate, hyaluronic acid or their salts)) or a bioactive molecule (insulin, erythropoietin, glucagon-like peptide 1, a melanocyte stimulating hormone, parathyroid hormone, growth hormone, calcitonin, interleukin-2, alpha1-antitrypsin, granulocyte/monocyte colony stimulating factor, granulocyte colony stimulating factor, T20, anti-tumor necrosis factor antibodies, interferon alpha, interferon beta, interferon gamma, lutenizing hormone, follicle-stimulating hormone, enkephalin, dalargin, kyotorphin, basic fibroblast growth factor, hirudin, hirulog, lutenizing hormone releasing hormone analog, brain-derived natriuretic peptide or neurotrophic factors)). (I) is a pharmaceutically active agent (a hormone, a growth factor, a neurotrophic factor, an anticoagulant, a bioactive molecule, a toxin, an antibiotic, an anti-fungal agent, an antipathogenic agent, an antigen, an antibody, an antibody fragment, an immunomodulator, a vitamin, an antineoplastic agent, an enzyme or a therapeutic agent). (I) is a

nucleic acid or a nucleic acid mimetic (a DNA or DNA-mimetic, a RNA or RNA-mimetic). The ionic liquid forming cation is imidazolium derivatives (1-R1-3-R2-imidazolinium (1) (preferably 1-ethyl-3-methylimidazolium, 1-butyl-3-methylimidazolium, 1-hexyl-3-methylimidazolium, 1-methyl-3-octylimidazolium, 1-methyl-3-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)-imidazolium, 1,3-dimethylimidazolium or 1,2-dimethyl-3-propylimidazolium)), pyridinium derivatives (1-R1-3-R2'-pyridinium (2) (preferably 3-methyl-1-propylpyridinium, 1-butyl-3-methylpyridinium or 1-butyl-4-methylpyridinium)), phosphonium compounds or tetralkylammonium compounds. The imidazolium derivative further comprises a halogen or an alkyl group substitution. The pyridinium derivative further comprises a halogen or an alkyl group substitution. (A) further comprises a hydrophobic carrier (free fatty acids, mono-glycerides, di-glycerides, tri-glycerides (preferably tricaprin), ethers (preferably benzyl benzoate) or cholesterol esters of fatty acids) and at least one protective agent (a protease inhibitor (aprotinin, Bowman-Birk inhibitor, soybean trypsin inhibitor, chicken ovomucoid, chicken ovoinhibitor, human pancreatic trypsin inhibitor, camostat mesilate, flavonoid inhibitors, antipain, leupeptin, p-aminobenzamidine, 4-(2-aminoethyl)benzenesulfonyl fluoride (AEBSF), N-(5-amino-1-chloroacetyl-pentyl)-4-methyl-benzenesulfonamide (TLCK), (4-amidino-phenyl)-methane-sulfonyl fluoride (APMSF), diisopropylfluorophosphate) (DFP), phenylmethylsulfonylfluoride (PMSF), poly(acrylate) derivatives, chymostatin, benzyloxycarbonyl-Pro-Phe-CHO, FK-448, sugar biphenylboronic acids complexes, beta-phenylpropionate, elastatinal, methoxysuccinyl-Ala-Ala-Pro-Val-chloromethylketone (MPCMK), ethylene diamine tetra acetic acid (EDTA), ****chitosan****-EDTA conjugates, amino acids, di-peptides, tripeptides, amastatin, bestatin, puromycin, bacitracin, phosphinic acid dipeptide analogs, alpha-aminoboronic acid derivatives, sodium glycocholate, 1,10-phenantroline, acivicin, L-serine-borate, thiorphan, or phosphoramidon). (A) further contains a poly anionic molecule (phytic acid) and a surface active agent (a poloxamer, solutol HS15, cremophore, phospholipids or bile acids). (A) is dissolved in an at least partially water soluble solvent (n-butanol, isoamyl (isopentyl) alchohol, iso-butanol, iso-propanol, propanol, ethanol, tert-butanol alcohols, polyols, dimethyl formamide, dimethyl sulfoxide, ethers, amides and/or esters). (A) contains one or more lyophilized components. (A) further comprises a mixture of at least two substances (a non-ionic detergent (a poloxamer (pluronic F-68) or solutol HS 15), an ionic detergent (a bile salt (taurodeoxycholate)), a protease inhibitor (aprotonin or soy bean trypsin inhibitor) or a reducing agent (N-acetyl-L-cysteine (NAC)). The antigen for vaccination is ****protective********antigen**** (used as a vaccine against ****Anthrax****) or Hepatitis B surface antigen (used as a vaccine against Hepatitis B). The at least one other constituent is a member of pluronic F-68, Aprotinin, Solutol HS-15, N-Acetyl Cysteine or Tricaprin. The effector further comprises a chemical modification. The chemical modification comprises the attachment of one or more polyethylene glycol residues to the effector. The ionic liquid forming cation is a constituent of a water soluble salt.

Preferred Methods: The translocation across a biological barrier (tight junctions or plasma membranes) occurs within a tissue of epithelial cells or endothelial cells. The biological barrier comprises gastro-intestinal mucosa or blood brain barrier. (A) is administered using parenteral (intraorbit) route to treat an ophthalmological disorder. The lyophilizing step alternatively comprises lyophilizing the effector and the counter ion with phytic acid or any other constituent of a pharmaceutical excipient or carrier. The reconstituting step alternatively comprises reconstituting the lyophilized materials and at least one other constituent of the composition in an aqueous, partially aqueous or organic solvent.

R1, R2= 1-12C alkyl

R2'= H or 1-12C alkyl

Title Terms/Index Terms/Additional Words: COMPOSITION; USEFUL; EFFECTOR; INSULIN; BIOLOGICAL; BARRIER; TREAT; DEMENTIA; PARKINSON; DISEASE; COMPRISE; COUNTER; ION

Class Codes
International Classification (+ Attributes)
IPC + Level Value Position Status Version
A61K-0031/00 A I R 20060101
A61K-0031/727 A I R 20060101
A61K-0031/737 A I R 20060101
A61K-0038/18 A I R 20060101
A61K-0038/19 A I R 20060101
A61K-0038/20 A I R 20060101
A61K-0038/21 A I R 20060101
A61K-0038/23 A I R 20060101
A61K-0038/24 A I R 20060101
A61K-0038/26 A I R 20060101
A61K-0038/27 A I R 20060101
A61K-0038/28 A I R 20060101
A61K-0038/29 A I R 20060101
A61K-0038/57 A I R 20060101
A61K-0038/58 A I R 20060101
A61K-0047/18 A I R 20060101
A61K-0009/00 A I R 20060101
A61K-0031/00 C I R 20060101
A61K-0031/726 C I R 20060101
A61K-0031/737 C I R 20060101
A61K-0038/18 C I R 20060101
A61K-0038/19 C I R 20060101
A61K-0038/20 C I R 20060101
A61K-0038/21 C I R 20060101
A61K-0038/23 C I R 20060101
A61K-0038/24 C I R 20060101
A61K-0038/26 C I R 20060101
A61K-0038/27 C I R 20060101
A61K-0038/28 C I R 20060101
A61K-0038/29 C I R 20060101
A61K-0038/55 C I R 20060101
A61K-0047/16 C I R 20060101
A61K-0009/00 C I R 20060101
ECLA: A61K-009/00M5, A61K-009/00M6, A61K-031/00, A61K-031/727, A61K-031/737 , A61K-038/18B+M, A61K-038/18C+M, A61K-038/19B+M, A61K-038/20B+M, A61K-038/21A+M, A61K-038/21B+M, A61K-038/21C+M, A61K-038/23+M, A61K-038/24+M, A61K-038/26+M, A61K-038/27+M, A61K-038/28+M, A61K-038/29+M , A61K-038/57+M, A61K-038/58+M, A61K-047/18D
US Classification, Current Main: 424-452000; Secondary: 514-054000, 514-056000
US Classification, Issued: 51454, 51456, 424452

File Segment: CPI
DWPI Class: A96; B04; B05; D16
Manual Codes (CPI/A-M): A12-V01; B01-D02; B04-A08C2; B04-A10G; B04-B01C1; B04-B03A; B04-B04C1; B04-C01; B04-C02; B04-C03B; B04-C03C; B04-H02B; B04-H04; B04-H05; B04-J03A; B04-J04A; B04-J04B; B04-J05J; B04-N02; B04-N04; B04-N06; B05-B01A; B05-B01J; B05-B01P; B07-H; B10-A08; B10-A09B; B10-A10; B10-A17; B10-B01B; B10-B02B; B10-C04B; B10-C04C; B10-C04E; B10-D03; B10-E04D; B10-G02; B12-M09; B14-A01; B14-A04; B14-B02; B14-C01;

B14-C03; B14-C06; B14-D01; B14-D01A; B14-D07C; B14-E12; B14-F01; B14-F02; B14-F03; B14-F04; B14-F07; B14-F08; B14-G02D; B14-G03; B14-H01B; B14-J01; B14-N01A; B14-N03; B14-N07; B14-N10; B14-N16; B14-P02; B14-S01; B14-S04; B14-S11; B14-S11A; B14-S13; B14-S16; D05-A02; D05-H07; D05-H11; D05-H12A

Original Publication Data by Authority

United States
Publication No. US 20050058702 A1 (Update 200526 B)
Publication Date: 20050317
Compositions capable of facilitating penetration across a biological barrier
Assignee: Ben-Sasson, Shmuel A., Jerusalem, IL (BENS-I)
Cohen, Einat, Jerusalem, IL (COHE-I)
Inventor: Ben-Sasson, Shmuel A., Jerusalem, IL
Cohen, Einat, Jerusalem, IL
Agent: MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, US
Language: EN (12 pages, 0 drawings)
Application: US 2003664989 A 20030917 (Local application)
Original IPC: A61K-31/727(A) A61K-9/20(B) A61K-9/48(B) A61K-31/737(B)
Current IPC: A61K-31/00(R,A,I,M,EP,20060101,20051008,A)
A61K-31/00(R,I,M,EP,20060101,20051008,C)
A61K-31/726(R,I,M,EP,20060101,20051008,C)
A61K-31/727(R,I,M,EP,20060101,20051008,A)
A61K-31/737(R,I,M,EP,20060101,20051008,A)
A61K-31/737(R,I,M,EP,20060101,20051008,C)
A61K-38/18(R,I,M,EP,20060101,20060722,A)
A61K-38/18(R,I,M,EP,20060101,20060722,C)
A61K-38/19(R,I,M,EP,20060101,20060722,A)
A61K-38/19(R,I,M,EP,20060101,20060722,C)
A61K-38/20(R,I,M,EP,20060101,20060722,A)
A61K-38/20(R,I,M,EP,20060101,20060722,C)
A61K-38/21(R,I,M,EP,20060101,20060722,A)
A61K-38/21(R,I,M,EP,20060101,20060722,C)
A61K-38/23(R,I,M,EP,20060101,20060722,A)
A61K-38/23(R,I,M,EP,20060101,20060722,C)
A61K-38/24(R,I,M,EP,20060101,20060722,A)
A61K-38/24(R,I,M,EP,20060101,20060722,C)
A61K-38/26(R,I,M,EP,20060101,20060722,A)
A61K-38/26(R,I,M,EP,20060101,20060722,C)
A61K-38/27(R,I,M,EP,20060101,20060722,A)
A61K-38/27(R,I,M,EP,20060101,20060722,C)
A61K-38/28(R,I,M,EP,20060101,20060722,A)
A61K-38/28(R,I,M,EP,20060101,20060722,C)
A61K-38/29(R,I,M,EP,20060101,20060722,A)
A61K-38/29(R,I,M,EP,20060101,20060722,C)
A61K-38/55(R,I,M,EP,20060101,20060722,C)
A61K-38/57(R,I,M,EP,20060101,20060722,A)
A61K-38/58(R,I,M,EP,20060101,20060722,A)
A61K-47/16(R,I,M,EP,20060101,20060722,C)
A61K-47/18(R,I,M,EP,20060101,20060722,A)
A61K-9/00(R,I,M,EP,20060101,20060722,A)
A61K-9/00(R,I,M,EP,20060101,20060722,C)
Current ECLA class: A61K-9/00M5 A61K-9/00M6 A61K-31/00 A61K-31/727 A61K-31/737 A61K-38/18B+M A61K-38/18C+M A61K-38/19B+M A61K-38/20B+M A61K-38/21A+M A61K-38/21B+M A61K-38/21C+M A61K-38/23+M A61K-38/24+M A61K-38/26+M A61K-38/27+M A61K-38/28+M A61K-38/29+M A61K-38/57+M A61K-38/58+M A61K-47/18D
Current US Class (main): 424-452000
Current US Class (secondary): 514-054000 514-056000
Original US Class (main): 424452

Original US Class (secondary): 51454 51456
Original Abstract: This invention relates to novel pharmaceutical compositions mixing one or more effectors (anionic impermeable molecules) with a counter ion to the effector (a liquid forming cation). The invention also relates to methods of treating or preventing diseases by administering pharmaceutical compositions to affected subjects.
Claim: We claim:
1.
1. A composition for the translocation of at least one effector across a biological barrier comprising a therapeutically effective amount of said at least one effector, and a counter ion to the at least one effector.

12/7/12 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

0013777709
WPI ACC NO: 2003-877105/200381
XRAM Acc No: C2003-247672
New polynucleotide vaccine composition comprising a nucleic acid sequence that encodes a Bacillus ****anthracis**** antigen, useful for eliciting a protective immune response against Bacillus ****anthracis****
Patent Assignee: FULLER J T (FULL-I); POWDERJECT RES LTD (POWD-N); SCHMALJOHN C S (SCHM-I)
Inventor: FULLER J; FULLER J T; SCHMALJOHN C; SCHMALJOHN C S
Patent Family (3 patents, 101 countries)

Patent Number	Kind	Date	Application Number	Kind	Date	Update	
WO 2003087378	A1	20031023	WO 2003GB1553	A	20030411	200381	B
US 20040082530	A1	20040429	US 2002371416	P	20020411	200429	E
			US 2003411205	A	20030411		
AU 2003224265	A1	20031027	AU 2003224265	A	20030411	200436	E

Priority Applications (no., kind, date): US 2002371416 P 20020411; US 2003411205 A 20030411

Patent Details

Number	Kind	Lan	Pg	Dwg	Filing Notes
WO 2003087378	A1	EN	65	0	

National Designated States,Original: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
Regional Designated States,Original: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

US 20040082530	A1	EN	Related to Provisional US 2002371416
AU 2003224265	A1	EN	Based on OPI patent WO 2003087378

Alerting Abstract WO A1
NOVELTY - A new polynucleotide vaccine composition comprises a nucleic acid sequence that encodes a ~Bacillus ****anthracis~********antigen**** and that is operatively linked to a promoter suitable for expression of the antigen in a mammalian cell.
DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

1.a particle acceleration device loaded with core carrier particles that are coated with the polynucleotide;

2.a hermetically sealed single unit dosage or multidose container adapted for use in a particle acceleration device and comprising core carrier particles that are coated with the polynucleotide;

3.a method for eliciting a protective immune response against

4.~Bacillus ****anthracis

5.~**** in a subject; and

6.a method ****for**** using

7.~Bacillus ****anthracis

8.~**** antigen to induce an immune response in a subject.

********ACTIVITY - Antibacterial. No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The polynucleotide vaccine composition is useful for eliciting a protective immune response against ~Bacillus ****anthracis~**** (claimed).

Technology Focus
BIOTECHNOLOGY - Preferred Composition: The polynucleotide vaccine composition is in particulate form. It further comprises an adjuvant component, an excipient, a vehicle or a transfection-facilitating agent. The adjuvant component is present in the composition in the form of a nucleic acid sequence, polypeptide, lipid, non-protein hormone or vitamin. It is a CpG sequence or a further nucleic acid sequence that encodes a polypeptide adjuvant. It comprises ****monophosphoryl********lipid**** ****A**** or saponin or its derivative. It comprises Quil-A. The nucleic acid sequence is present in a plasmid vector. The nucleic acid sequence encodes an antigen obtained or derived from the ****Protective**** ****Antigen**** of ~Bacillus ****anthracis~****. ****The**** antigen encoded by the nucleic acid sequence is substantially homologous to the full-length ****Protective********Antigen********protein****. ****The**** second nucleic acid sequence that encodes a leader signal peptide is operatively linked to the nucleic acid sequence that encodes a ~Bacillus ****anthracis~**** antigen, where ****the**** nucleic acid sequences are operatively linked to a promoter suitable for expression in a mammalian cell and the leader signal peptide provides for the secretion of the encoded antigen. The nucleic acid sequence is coated onto a core carrier particle, having an average diameter of 0.1-10microm and comprising a metal, which is gold. The leader signal peptide is the tissue plasminogen activator leader signal peptide. The vaccine composition is administered using a particle-mediated delivery technique. It is administered directly into skin or muscle tissue. A second vaccine composition is administered to the subject. The second vaccine composition is an anti-~Bacillus ****anthracis~**** vaccine containing the peptide ****form**** of the ****Protective********Antigen**** from ~Bacillus ****anthracis~****. The ****second********vaccine**** composition is administered ****to**** the subject in a boosting step. The first and second vaccine compositions are administered concurrently to the same site in the subject.
Preferred Methods: Eliciting a protective immune response against ~Bacillus ****anthracis~**** in a subject comprises administering the vaccine composition ****to**** the subject, where upon introduction to the subject, the nucleic acid sequence is expressed to provide the ~Bacillus ****anthracis~**** antigen. Using ~Bacillus ****anthracis~**** antigen to induce an immune response ****in**** a subject comprises:

1.********providing an expression cassette containing a nucleic acid sequence encoding the ****Protective**** ****Antigen**** from

2.~Bacillus ****anthracis

3.~**** operatively linked to control sequences that direct expression of the ****Protective**** ****Antigen**** ****when**** introduced into tissue ****of**** the subject; and

4.administering the expression cassette to tissue of the ****subject**** ****such**** that the ****Protective**** ****Antigen**** is expressed in an amount sufficient to induce the immune response in the subject.

**********The method also comprises:

1.providing an expression cassette containing a first nucleic acid sequence encoding the ****Protective**** ****Antigen**** from

2.~Bacillus ****anthracis

3.~**** and a second nucleic acid sequence that encodes a leader signal peptide, where the first and second nucleic acid ****sequences**** ****are**** operatively linked to ****control**** sequences that direct expression of the ****Protective**** ****Antigen**** when introduced into tissue of the subject and the leader signal peptide provides for the secretion of the encoded ****Protective**** ****Antigen****; and

4.administering the ****expression**** ****cassette**** to tissue of the subject such that the ****Protective**** ****Antigen**** is expressed in an amount sufficient to induce the ****immune**** ****response**** in the subject.

Title Terms/Index Terms/Additional Words: NEW; POLYNUCLEOTIDE; VACCINE; COMPOSITION; COMPRISE; NUCLEIC; ACID; SEQUENCE; ENCODE; BACILLUS; ANTIGEN; USEFUL; ELICIT; PROTECT; IMMUNE; RESPOND

Class Codes
International Classification (+ Attributes)
IPC + Level Value Position Status Version
A61K-0039/00 A N R 20060101
A61K-0039/07 A I R 20060101
C07K-0014/32 A I R 20060101
C12N-0015/31 A I R 20060101
A61K-0039/00 C N R 20060101
A61K-0039/07 C I R 20060101
C07K-0014/195 C I R 20060101
C12N-0015/31 C I R 20060101
ECLA: A61K-039/07, C07K-014/32
ICO: K61K-039:00, K61K-039:53, K61K-039:54, K61K-039:555B11, K61K-039:555B13, K61K-039:555B5, K61K-039:555B7, M07K-207:00
US Classification, Current Main: 514-044000
US Classification, Issued: 51444

File Segment: CPI
DWPI Class: B04; D16
Manual Codes (CPI/A-M): B04-A07E; B04-B01B; B04-B04C1; B04-C01; B04-E02; B04-E03; B04-E08; B05-A03B; B11-C04; B11-C06; B14-A01B; B14-G01; B14-S11B; D05-A01A5; D05-H07; D05-H10; D05-H12A; D05-H12E

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Australia
Publication No. AU 2003224265 A1 (Update 200436 E)
Publication Date: 20031027
Assignee: POWDERJECT RES LTD (POWD-N)
Inventor: SCHMALJOHN C
  FULLER J
Language: EN
Application: AU 2003224265 A 20030411 (Local application)
Priority: US 2002371416 P 20020411
Related Publication: WO 2003087378 A (Based on OPI patent)
Current IPC: A61K-39/00(R,N,M,EP,20060101,20051008,A)
    A61K-39/00(R,N,M,EP,20060101,20051008,C)
    A61K-39/07(R,I,M,EP,20060101,20051008,A)
    A61K-39/07(R,I,M,EP,20060101,20051008,C)
    C07K-14/195(R,I,M,EP,20060101,20051008,C)
    C07K-14/32(R,I,M,EP,20060101,20051008,A)
    C12N-15/31(R,I,M,WO,20060101,20060521,A)
    C12N-15/31(R,I,M,WO,20060101,20060521,C)
Current ECLA class: A61K-39/07 C07K-14/32
Current ECLA ICO class: K61K-39:00 K61K-39:53 K61K-39:54 K61K-39:555B11
    K61K-39:555B13 K61K-39:555B5 K61K-39:555B7 M07K-207:00

United States
Publication No. US 20040082530 A1 (Update 200429 E)
Publication Date: 20040429
Nucleic acid immunization
Assignee: Schmaljohn, Connie S., Fort Detrick, MD, US (SCHM-I)
  Fuller, James T., Middleton, WI, US (FULL-I)
Inventor: Schmaljohn, Connie S., Fort Detrick, MD, US
  Fuller, James T., Middleton, WI, US
Agent: Alisa Harbin, Chiron Corporation, P.O. Box 8097, Emeryville, CA, US
Language: EN
Application: US 2002371416 P 20020411 (Related to Provisional)
  US 2003411205 A 20030411 (Local application)
Original IPC: A61K-48/00(A)
Current IPC: A61K-39/07(R,A,I,M,EP,20060101,20051008,A)
    A61K-39/07(R,I,M,EP,20060101,20051008,C)
Current ECLA ICO class: K61K-39:53
Current US Class (main): 514-044000
Original US Class (main): 51444
Original Abstract: Recombinant nucleic acid molecules are described. The
    molecules have a sequence or sequences encoding an antigen from
    ~Bacillus anthracis~. Vectors and compositions containing these
    molecules are also described. Methods for eliciting an immune response
    using these molecules and compositions are also described.
Claim: What is claimed is:
  1.
1. A polynucleotide vaccine composition comprising a nucleic acid
        sequence that encodes a ~Bacillus anthracis ~antigen, wherein said
        nucleic acid sequence is operatively linked to a promoter suitable
        for expression of the antigen in a mammalian cell.

WIPO
Publication No. WO 2003087378 A1 (Update 200381 B)
Publication Date: 20031023
**NUCLEIC ACID IMMUNIZATION
  IMMUNISATION D'ACIDES NUCLEIQUES**
Assignee: POWDERJECT RESEARCH LIMITED, 4 Robert Robinson Avenue, The Oxford
    Science Park, Oxford OX4 4GA, GB Residence: GB Nationality: GB (POWD-N)
Inventor: SCHMALJOHN, Connie, US Army Medical Research Institute of
    Infectious D, isease, 1425 Porter Street, Fort Detrick, MD 21702-5011,
    US

FULLER, James, 585 Science Drive, Madison, WI 53711, US
Agent: WOODS, Geoffrey, Corlett, J.A. Kemp Co., 14 South Square, Gray's Inn, London WC1R 5JJ, GB
Language: EN (65 pages, 0 drawings)
Application: WO 2003GB1553 A 20030411 (Local application)
Priority: US 2002371416 P 20020411
Designated States: (National Original) AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
(Regional Original) AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
Original IPC: C12N-15/31(A) A61K-39/07(B) C12N-15/11(B)
Current IPC: A61K-39/00(R,A,N,M,EP,20060101,20051008,A)
A61K-39/00(R,N,M,EP,20060101,20051008,C)
A61K-39/07(R,I,M,EP,20060101,20051008,A)
A61K-39/07(R,I,M,EP,20060101,20051008,C)
C07K-14/195(R,I,M,EP,20060101,20051008,C)
C07K-14/32(R,I,M,EP,20060101,20051008,A)
C12N-15/31(R,I,M,WO,20060101,20060521,A)
C12N-15/31(R,I,M,WO,20060101,20060521,C)
Current ECLA ICO class: K61K-39:00 K61K-39:53 K61K-39:54 K61K-39:555B11 K61K-39:555B13 K61K-39:555B5 K61K-39:555B7 M07K-207:00
Original Abstract: Recombinant nucleic acid molecules are described. The molecules have a sequence or sequences encoding an antigen from ~Bacillus anthracis~. Vectors and compositions containing these molecules are also described. Methods for eliciting an immune response using these molecules and compositions are also described.
La presente invention a trait a des acides nucleiques recombinants. Les molecules presentent une ou des sequences codant pour un antigene derive de ~Bacillus~ ~anthracis~. L'invention a trait egalement a des vecteurs et des compositions contenant ces molecules. L'invention concerne en outre des procedes pour declencher une reponse immunitaire mettant en oeuvre ces molecules et compositions.

12/7/13 (Item 4 from file: 351)
DIALOG(R)File 351:Derwent WPI

0012447406
WPI ACC NO: 2002-393007/200242
Related WPI Acc No: 2002-236307
XRAM Acc No: C2002-110489
New recombinant asporogenic Bacillus ****anthracis**** strain useful for producing a ****protective**** ****antigen**** for use in vaccines against human ****anthrax****
Patent Assignee: FARCHAUS J W (FARC-I); FRIEDLANDER A M (FRIE-I); IVINS B (IVIN-I); US SEC OF ARMY (USSA); WELKOS S L (WELK-I); WORSHAM P (WORS-I)
Inventor: FARCHAUS J W; FRIEDLANDER A M; IVINS B; WELKOS S L; WORSHAM P
Patent Family (2 patents, 1 countries)

Patent Number	Kind	Date	Application Number	Kind	Date	Update	
US 20020034512	A1	20020321	US 1994346238	A	19941123	200242	B
			US 2000520215	A	20000307		
US 6387665	B1	20020514	US 2000520215	A	20000307	200242	E

Priority Applications (no., kind, date): US 1994346238 A 19941123; US 2000520215 A 20000307
Patent Details

Number	Kind	Lan	Pg	Dwg	Filing Notes
US 20020034512	A1	EN	6	0	Division of application US 1994346238

Alerting Abstract US A1

NOVELTY - Recombinant asporogenic ~Bacillus ****anthracis**** ~ ****strain**** (I) that is derived from DeltaSterne-1(pPA102) and shows inability to bind the dye when grown on Congo Red Agar is new.

DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

1.a composition comprising (I) in a growth medium;

2.a vaccine comprising a ****protective**** ****antigen**** produced by (****I****).

********ACTIVITY - Antibacterial.

No supporting data available.

MECHANISM OF ACTION - Vaccine (claimed).

No supporting data available.

USE - (I) is useful for producing a ****protective********antigen**** (****PA****) for use in ****vaccines********against********human**** ****anthrax****.

********ADVANTAGE - (I) is asporogenic and produces a ****protective**** ****antigen**** (****PA****) capable of eliciting ****high********anti****-****PA**** antibody titers.

Technology Focus

BIOTECHNOLOGY - Preparation: A 6 kb Bam HI fragment harboring the ****protective********antigen**** (****PA****) structural gene isolated from the endogenous Sterne plasmid pX01 was ligated into plasmid pBR322 and cloned into ~Escherichia coli ~ bacteria. From the resultant recombinant plasmid pSE36, the 6 kb fragment was then subcloned into the gram positive vector pUB110 using the Bam HI restriction site. The resulting plasmid was transformed into ~B. subtilis ~ IS53 and two stable ****PA**** producing, kanamycin resistant ****isolates**** were found (pPA101 and pPA102). Subsequent analysis of the plasmids revealed that both had suffered spontaneous deletions. The pPA102 was found to have lost 4 2 kb of DNA from 363 bp 3' of the kanamycin resistance gene to approximately 164 bp 5' of the start of the ****PA**** structural gene. The ****plasmid**** was then electrotransformed into DeltaSterne-1 and transformants were selected for kanamycin resistance. Transformants displaying a stable ****PA****+, kanamycin resistant, (LF-, ****EF****-, capsule-) phenotype were selected. This strain, DeltaSterne-1(pPA102), was then subjected to Congo Red agar selection for mutants displaying an inability to bind the dye. The selected isolate, now designated DeltaSterne-1(pPA102)CR4 was further subcultured three times to insure that a single clone was isolated.

Title Terms/Index Terms/Additional Words: NEW; RECOMBINATION; ASPOROGENIC; BACILLUS; STRAIN; USEFUL; PRODUCE; PROTECT; ANTIGEN; VACCINE; HUMAN; ****ANTHRAX****

Class Codes

International Classification (+ Attributes)

IPC + Level	Value	Position	Status	Version
C12N-0015/75	A	I	R	20060101
C12N-0015/74	C	I	R	20060101

ECLA: C12N-015/75, C12R-001/07

US Classification, Current Main: 424-184100, 435-071100; Secondary: 424-184100, 424-234100, 424-246100, 435-069100, 435-069400, 435-252300, 435-252310, 435-320100, 435-485000, 530-350000

US Classification, Issued: 424184.1, 424234.1, 424246.1, 530350, 43569.1, 43571.1, 43569.1, 43569.4, 435320.1, 435172.1, 435172.3, 435252.3,

435200.1, 435252.31, 530350, 424184.1, 424234.1, 424246.1

File Segment: CPI
DWPI Class: B04; C06; D16
Manual Codes (CPI/A-M): B04-F10B1E; B04-N03; B14-A01B; B14-S11B; C04-F10B1E ; C04-N03; C14-A01B; C14-S11B; D05-H07; D05-H14A1

Original Publication Data by Authority

United States
Publication No. US 20020034512 A1 (Update 200242 B)
Publication Date: 20020321
METHOD OF MAKING A VACCINE
Assignee: Ivins, Bruce, Frederick, MD, US (IVIN-I)
Worsham, Patricia, Jefferson, MD, US (WORS-I)
Friedlander, Arthur M, Gaithersburg, MD, US (FRIE-I)
Farchaus, Joseph W, Frederick, MD, US (FARC-I)
Welkos, Susan L, Frederick, MD, US (WELK-I)
Inventor: Ivins, Bruce, Frederick, MD, US
Worsham, Patricia, Jefferson, MD, US
Friedlander, Arthur M, Gaithersburg, MD, US
Farchaus, Joseph W, Frederick, MD, US
Welkos, Susan L, Frederick, MD, US
Agent: John F Moran, Office of Command Judge Advocate, HQ. USAMRDC Department of the Army, Fort Detrick, Frederick, MD, US
Language: EN (6 pages, 0 drawings)
Application: US 1994346238 A 19941123 (Division of application)
US 2000520215 A 20000307 (Local application)
Original IPC: A61K-39/07(A)
Current IPC: C12N-15/74(R,A,I,M,EP,20060101,20051008,C) C12N-15/75(R,I,M,EP,20060101,20051008,A)
Current ECLA class: C12N-15/75 C12R-1/07
Current US Class (main): 424-184100
Current US Class (secondary): 424-234100 424-246100 435-069100 530-350000
Original US Class (main): 424184.1
Original US Class (secondary): 424234.1 424246.1 530350 43569.1
Original Abstract: A method of making a vaccine from a protective antigen. The protective antigen is useful against ~Bacillus anthracis~. The protective antigenis produced by an asporogenic organism which overpoduces the desired antigen. The asporogenic organism is a recombinant asporogenic ~B. anthracis~. The recombinant asporogenic ~B. anthracis ~was derived from a DeltaSterne-1(pPA102) strain of bacteria and binds to dye when grown on Congo Red Agar.
Claim:
1.
1. A recombinant asporogenic ~B. anthracis ~derived from DeltaSterne-1(pPA102) which shows inability to bind the dye when grown on Congo Red Agar.
Publication No. US 6387665 B1 (Update 200242 E)
Publication Date: 20020514
Method of making a vaccine for anthrax.
Assignee: The United States of America as represented by the Secretary of the Army, Washington, DC, US (USSA)
Inventor: Ivins, Bruce, Frederick, MD, US
Worsham, Patricia, Jefferson, MD, US
Friedlander, Arthur M., Gaithersburg, MD, US
Farchaus, Joseph W., Frederick, MD, US
Welkos, Susan L., Frederick, MD, US
Agent: Arwine; Elizabeth
Moran; John Francis

Harris; Charles H.
Language: EN
Application: US 2000520215 A 20000307 (Local application)
Original IPC: C12P-21/04(A)
Current IPC: C12N-15/74(R,A,I,M,EP,20060101,20051008,C)
C12N-15/75(R,I,M,EP,20060101,20051008,A)
Current ECLA class: C12N-15/75 C12R-1/07
Current US Class (main): 435-071100
Current US Class (secondary): 424-184100 424-234100 424-246100 435-069100
435-069400 435-252300 435-252310 435-320100 435-485000 530-350000
Original US Class (main): 43571.1
Original US Class (secondary): 43569.1 43569.4 435320.1 435172.1 435172.3
435252.3 435200.1 435252.31 530350 424184.1 424234.1 424246.1
Original Abstract: A method of making a vaccine for anthracis that inolves a bacterial expression system and production and use of protective antigen (PA) against ~Bacillus anthracis~. The PA immunogen is useful in a vaccine against human anthrax. The PA can be produced by an asporogenic organism which produces the desired antigen, which is then harvested from the supernatant.
Claim:
1.A method of making a vaccine comprising: incorporating a protective antigen produced by recombinant asporogenic
~B. anthracis~with a
pharmaceutically acceptable carrier, wherein said recombinant asporogenic ~B. anthracis ~was isolated from a DeltaSterne-1(pPA102) strain of bacteria and said recombinant asporogenic ~B. anthracis ~does not have the ability to bind a dye when grown on Congo Red Agar.

12/7/14 (Item 1 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts

0002034072 IP ACCESSION NO: 4618090
Immune correlates of protection against ****anthrax****

Fowler, K; McBride, BW; Turnbull, PCB; Baillie, LWJ
Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wilts SP4 0JG, UK

Journal of Applied Microbiology, v 87, n 2, p 305, August 1999
PUBLICATION DATE: 1999

PUBLISHER: Blackwell Science Ltd., Osney Mead Oxford OX2 0EL UK,
[URL:http://www.blacksci.co.uk]

CONFERENCE:
3rd International Conference on Anthrax, Plymouth (UK), 7-10 Sep 1998

DOCUMENT TYPE: Journal Article; Summary
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 1364-5072
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:
Bacillus ****anthracis**** ****protective**** ****antigen**** (****PA****) has been produced from a recombinant B. subtilis and its efficacy, when combined with the Ribi adjuvant (****MPL****-TDW-CWS) or alhydrogel, has been compared with that of the licensed UK human vaccine, in guinea pigs

challenged with aerosolized Ames strain spores. Recombinant ****PA**** combined with the Ribi adjuvant performed as well as ****PA**** from B. ****anthracis**** cultures in previous reports (Ivins and Welkos 1986; Ivins et al. 1990; Turnbull et al. 1991; Jones et al. 1996; McBride et al. 1998) giving protection in 100% of animals exposed to the highest challenge dose of the Ames strain of B. ****anthracis**** that can be administered practically (retained lung doses of approximately 10 super(6) spores). In attempts at identifying markers of protection in immunized individuals, rPA in combination with the Ribi adjuvant induced a marker IgG sub(2) response in guinea pigs with no significant differences in IgG sub(1) levels when compared with other vaccine formulations (McBride et al. 1998). In BALBc mice, rPA with the Ribi adjuvant induced a higher IgG sub(2a) response compared with rPA with anhydrogel and the human vaccine. To examine the role of anti-****PA****-specific antibodies in protection, guinea pig sera is being passively transferred into guinea pigs and SCID mice, followed by protection. Similarly, B- and T-lymphocytes from immunized BALB/c mice are being separately and passively transferred into SCID mice with subsequent challenge. The neutralizing ability of the ****PA****-specific antibodies is being studied using an in vitro macrophage lysis assay.
? ds

Set	File	Items	Description
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	347	0	
	144	11	
	35	1	
	5	15	
	74	0	
	71	14	
	6	3	
	351	41	
	24	13	
	136	0	
	399	2	
	315	1	
	73	26	
	34	28	
	434	0	
S1		488	((PROTECTIVE (W) ANTIGEN) OR PA) AND ((MONOPHOSPHORYL (W)LIPID(W)A) OR MPL)
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	144	6	
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	5	11	
	74	0	
	71	7	
	6	3	
	351	5	
	24	10	
	136	0	
	399	0	
	315	1	
	73	17	
	34	17	
	434	0	
S2		275	S1 NOT PY>2005
	155	0	
	347	0	
	144	0	
	35	0	
	5	0	

	74	0	
	71	0	
	6	0	
	351	0	
	24	0	
	136	0	
	399	0	
	315	0	
	73	0	
	34	0	
	434	0	
S3		0	((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHIOTOSAN)
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	347	1	
	144	44	
	35	3	
	5	56	
	74	4	
	71	20	
	6	0	
	351	258	
	24	19	
	136	3	
	399	10	
	315	4	
	73	127	
	34	116	
	434	0	
S4		1180	((PROTECTIVE (W) ANTIGEN) OR PA) AND (CHITOSAN)
	155	144	
	347	1	
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	35	0	
	5	18	
	74	0	
	71	7	
	6	0	
	351	32	
	24	4	
	136	2	
	399	1	
	315	3	
	73	41	
	34	35	
	434	0	
S5		305	S4 NOT PY>2005
	155	144	
	347	1	
	144	13	
	35	0	
	5	5	
	74	0	
	71	1	
	6	0	
	351	32	
	24	1	
	136	0	
	399	1	
	315	3	
	73	25	
	34	15	
	434	0	

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S6                241   RD S5  (unique items)
      155         198
      347           0
      144           0
       35           0
        5           0
       74           0
       71           0
        6           2
      351           5
       24           1
      136           0
      399           0
      315           1
       73           5
       34           7
      434           0
S7                219   RD S2  (unique items)
      155         198
      347           0
      144           0
       35           0
        5           0
       74           0
       71           0
        6           2
      351           5
       24           1
      136           0
      399           0
      315           1
       73           5
       34           7
      434           0
S8                219   RD S2  (unique items)
      155           0
      347           0
      144           0
       35           0
        5           0
       74           0
       71           0
        6           0
      351           0
       24           0
      136           0
      399           0
      315           0
       73           0
       34           0
      434           0
S9                  0   S6 AND S7
      155         342
      347           1
      144          13
       35           0
        5           5
       74           0
       71           1
        6           2
      351          37
       24           2
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      136          0
      399          1
      315          4
       73         30
       34         22
      434          0
S10               460   S6 OR S7
      155          6
      347          0
      144          0
       35          0
        5          0
       74          0
       71          0
        6          1
      351          3
       24          1
      136          0
      399          0
      315          0
       73          0
       34          0
      434          0
S11                11   S10 AND (ANTRAX OR ANTHRACIS)
      155          7
      347          0
      144          1
       35          0
        5          0
       74          0
       71          0
        6          1
      351          4
       24          1
      136          0
      399          0
      315          0
       73          0
       34          0
      434          0
S12                14   S10 AND (ANTHRAX OR ANTHRACIS)
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       30jan12 11:17:07 User226352 Session D1340.2
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    $51.03  Estimated cost File73
   $109.60  Estimated cost File34
     $3.46  Estimated cost File434
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